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CLASSIFICATION OF OCULAR PATHOLOGY

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Any collection of histologic sections requires adequate cataloging to render it useful for study and reference. A classification is required for this cataloging or cross-indexing, and one based on clinical findings will not suffice for pathologic changes. To meet this need with respect to pathologic material from ocular lesions, a purely utilitarian classification has been evolved by the author during the past eighteen years. Begun as a skeleton outline, it has been gradually expanded as the needs arose and in its present form seems to answer the requirements of the department of pathology of the Institute of Ophthalmology. Since there have been requests for copies of it from time to time, it is probably of sufficient interest to warrant its publication.

Formerly one classification and index was used for globes and another for biopsy tissue and specimens other than globes. It seemed advisable to combine the two, however, and the classification now in use and reported herewith includes every sort of tissue removed from the eye and its surrounding parts. Notes have been appended to certain subheadings the meaning of which may not be entirely clear.

The section from a single globe may require the listing of any number of pathologic changes or diagnoses. The following is an illustrative case:

1. Tumor of Choroid: Melanoma—malignant
2. Inflammations: Endophthalmitis—following necrosis of tumor
3. Glaucoma: Secondary—to tumor
4. Congenital Anomaly: Schwalbe's ring
5. Congenital Anomaly: Intrascleral nerve loop
6. Iris: Necrosis

Atrophy of Globe [1]

Following ectogenous inflammation
Following endogenous inflammation

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1. Atrophy of the globe may follow an injury or an operation and still be the result of an ectogenous infection, but this relationship cannot always be established with certainty.

Following injury
Following operation

Cataract

Complicated:
- To drugs
  - Dinitrophenol
- To glaucoma
- To inflammation
- To operation
- To radiation
- To trauma
- To tumors
- Idiopathic

Congenital

Senile:
- Incipient
- Mature
- Hypermature

Choroid

Angioid streaks
Chorioretinal adhesions [2]
Choroiditis

Detachment: [3]
- Following contracture
- Following hemorrhage
- Following inflammation
- Following injury
- Following operation

Excrescences of lamina vitrea: [4]
- Pathologic (see also *Senile Changes*)

Fat emboli
Hemorrhage

2. Chorioretinal adhesions mean any adhesions between the choroid and the retina from whatever cause. Subdivisions under this heading have not proved practical.

3. A detachment may follow contracture of scar tissue and still be due to hemorrhage, inflammation, operation or injury, but it is sometimes difficult to be specific.

4. The term excrescences of lamina vitrea is used instead of drusen. Those spoken of as "pathologic" are listed here; all others are listed under *"Senile Changes."*

Ciliary Body

Excrescences of lamina vitrea
Proliferation of epithelium

Comparative Anatomy

Cat
Dog
Monkey, etc.

Congenital Anomalies

Aberrant optic nerve fibers
Anterior synechia
Ciliary processes on iris

Coloboma:
- Of globe
- Of iris
- Of optic nerve

Cyclops
Dislocation of lens
Embryonic filtration angle
Hyaloid system
Intrascleral nerve loop
Iris processes
Major arterial circle in iris
Marginal sinus [5]
Medullated nerve fibers
Melanosis oculi
Microphthalmos
Misplaced cilia
Peripheral iris nob

Pigmentation:
- Of optic nerve
- Of pectinate ligament

Pupillary membrane
Retinal detachment
Retinal folds
Retinal rosettes

5. Marginal sinus means a patent ring sinus of Szily near the pupillary margin.

Retrobulbar cyst
Schwalbe's ring
Thinned sclera
Vascular capsule of lens

Conjunctiva

Concretion

Conjunctivitis:
- Nonspecific
- Parinaud's
- Trachoma
- Vernal

Filtering cicatrix [6]
Lymphangiectasis
Melanosis
Pemphigus
Phlyctenule
Pigmentation of limbus
Pinguecula
Xerosis

Cornea

Abscess:
- Of posterior wall
- Ring

Aplanatio
Blood staining

Deposits:
- Endothelium
- Lens material
- Leukocytes
- Pigment
- Uveal tissue

Descemet's membrane:
- Detachment
- Regeneration

6. Filtering cicatrix includes the redundant tissue that is sometimes excised over the site of a filtering operation.

- Rupture
- Wrinkling

Duplication of epithelium [7]

Dystrophy

Ectasia

Fistula

Keratinization

Keratitis:

- Accompanying uveitis
- Actinic
- Band
- Bullous
- From new growth
- From injury to Descemet's membrane
- Herpes febrilis corneae
- Herpes zoster
- Idiopathic
- Neuroparalytic
- Traumatic

Keratoconus

Leukoma adherens

Membrane on posterior surface

Necrosis

Pannus:

- Degenerativus
- Eczematous
- Radiation
- Secondary [8]
- Trachomatous

Phacocele

Phthisis

Pigment granules between posterior corneal lamellae

Pigmentation of epithelium

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7. Duplication of epithelium means a double thickness of epithelium usually seen in glaucomatous eyes due to the fact that the original layer became detached from Bowman's membrane but left a few basal cells from which a new layer grew.

8. Secondary pannus includes any vascularized membrane extending over the surface of the cornea to some lesion on the cornea.

Pseudopterygium
Pterygium
Rhytitosis
Scars
Sclerosis
Sequestration
Transplants

Ulcers:
- Actinic
- Atheromatous
- Catarrhal
- Complicating glaucoma
- Eczematous
- From exposure
- From lye
- Herpes zoster
- Idiopathic
- Marantic
- Mooren's
- Neuroparalytic
- Posterior
- Serpens
- Specific
  - Aspergillus
  - Bacillus diphtheriae
  - Bacillus pyocyaneus
  - Gonorrheal
  - Pneumonococcus
  - Trachomatous
- Traumatic

Cysts

Of anterior chamber (epithelization)
Of caruncle

Of ciliary body:
- Idiopathic
- Grafe blebs

Of conjunctiva
Of cornea
Of iris
Of lacrimal gland

Of lid and brow:
- Epithelial
- Sebaceous
- Sweat gland

Of limbus
Of optic nerve
Of orbit (see also *Congenital Anomalies:* Retrobulbar cyst)
Of retina
- In general
- In macula
- In periphery

Of sclera
Of skin

Degenerations

Amyloid:
- Of conjunctiva

Bone

Calcium:
- In choroid
- In ciliary body
- In cornea
- In lens
- In retina
- In sclera

Cholesterol

Fat:
- In cornea

Hyalin:
- In cornea
- In retina
- In sclera

Embryo

Embryology

Foreign Bodies [9]

Brass or copper
Carbon

9. In most instances, of course, only the bed of the foreign body was seen, not the body itself.

Cilia
Cotton
Glass
Iron
Potassium hydroxide
Powder
Stone
Unclassified
Wood

Glaucoma

Buphthalmos [10]
Hydrophthalmos [11]

Primary:

Absolute
Acute
Chronic

Secondary:

To detachment of retina
To dislocated lens
To hemorrhage in choroid
To inflammation
To injuries
To occlusion of central vein
To operations
To perforated ulcer
To radiation
To trabecular obstruction
To tumors

Spontaneous perforation of globe

Inflammations [12]

Endophthalmitis:

Following injuries
Following necrosis of tumors

10. The term buphthalmos is employed for an enlarged ectatic eye of an infant or child from any cause of secondary glaucoma.

11. The term hydrophthalmos is used for the same condition caused by a congenital malformation of the filtration angle.

12. Inflammations includes inflammation involving more than one structure of the eye. If only one structure is involved, the inflammation is listed under the name of the structure, such as "Choroid," "Sclera," etc.

Following operations
Following ulcers
Idiopathic
Metastatic
Foreign body reaction
Granulation tissue

Inflammatory tissue:

Acute
Chronic
Procainoma [13]

Panophthalmitis:

Ectogenous
Endogenous
From necrosis of tumor

Uveitis:

Endogenous
Following injury
Following operation
From detachment of retina
From herpes zoster
From lens antigen
From necrosis of tumor

Injuries

Burns:

Actinic
Chemical
Contusions
Cyclodialysis

Evulsion:

Optic nerve

Hemorrhage:

In choroid
Retinal—of newborn
Incised wounds
Inversion or recession of iris
Iridodialysis or aniridia
Laceration

13. Procainoma includes the localized granuloma that sometimes results from the injection of old or contaminated procaine hydrochloride.

Luxation of lens:
- Into anterior chamber
- Into vitreous
- Subconjunctival

Perforations
Retinitis sclopetaria

Rupture of globe:
- Direct
- Indirect

Rupture:
- Of retina
- Of lens capsule

Siderosis
Subluxation of lens

Wound:
- Of ciliary body
- Of lens
- Of retina

Iris

Atrophy:[14]
- With proliferation
- Without proliferation

Descemet's membrane on anterior surface
Ectropion uvea
Entropion uvea
Indentation by ciliary processes
Iris in wound without repair
Membrane on posterior surface
Necrosis
Occlusion of pupil
Russell bodies
Seclusion of pupil (bombé)

Lacrimal Apparatus

Dacryoadenitis
Dacryocystitis

14. Atrophy with proliferation designates that kind of atrophy in which the normal stroma is replaced by fibrous tissue, and atrophy without proliferation that kind in which the stroma has disappeared and left a hole or rarefied area.

Lid

Blepharochalasis
Chalazion
Dermatitis
Keratosis
Melanosis
Molluscum contagiosum
Tarsitis
Xanthelasma

Muscles

Congenital fibrosis

Myositis:
  Idiopathic
  In hyperthyroidism (see *Systemic Diseases*)

Tenosynovitis:
  Idiopathic
Zenker's waxy degeneration

Myopia

Myopia

Normal [15]

Anterior sector
Bone
Cartilage
Caruncle
Choroid
Ciliary ganglion
Conjunctiva
Connective tissue
Cornea
Entire globe
Fat
Iris
Lacrimal gland
Lamina cribrosa

15. Whenever separate structures, such as iris, choroid, retina, macula and others, are listed under "Normal," it means that they are particularly good for study. They may be in globes not otherwise normal, as an iris in a globe with a malignant melanoma of the choroid, etc.

Lids
Lymph node
Macula
Meninges
Muscle
Nerve
Optic nerve and pathways
Posterior sector
Postmortem changes
Punctum and canaliculus
Retina
Sclera
Skin
Sympathetic ganglion

Vitreous:

Ligamentum hyaloidea capsularis

Operations

Cataract
Cyclodialysis
Discission

For retinal detachment:

Diathermy
Gonin's operation
Guist's operation

Iridectomy
Iridotasis
Keratoplasty
Lagrange
Needling
Paracentesis
Sclerotomy

Tattooing of cornea:

By chemicals
By ink
By unknown substance

Trephine

Optic Nerve

Atrophy:

Primary
Secondary to arteriosclerosis

Secondary to choroiditis
Secondary to glaucoma
Secondary to optic neuritis
Secondary to papilledema
Secondary to pressure in orbit or cranium

Conus:
Temporal
Corpora arenacea
Disappearance of cupping:
From edema
From proliferation of glial tissue
Fatty degeneration
Hyaline bodies [16]
Miscellaneous

Neuritis:
Idiopathic
Secondary to inflammation in anterior part of globe

Papilledema:
Following hypotony
Following increased intracranial pressure
Following intracranial inflammation
Following tumor of choroid
Following tumor of orbit
Experimental

Pigmentation:
Acquired
Congenital (see *Congenital Anomalies*)
Proliferation of lamina cribrosa
Schnabel spaces
Supertraction of retina

Orbit

Cellulitis
Orbital granuloma (pseudotumor)

Phthisis Bulbi

Following inflammation
Following trauma
Following tumor

16. The term hyaline bodies is employed to designate what is usually spoken of as drusen of the optic nerve.

Retina

Atrophy:
- From arteriosclerosis
- From choroidal lesion
- From glaucoma

Deposits on internal surface

Detachment:
- Following chorioretinitis
- Following contracture
- Following cyst
- Following dialysis
- Following hemorrhage
- Following hole
- Following leukemia
- Following myopia
- Following nephritis
- Following papilledema
- Following trauma
- Idiopathic
- In glaucoma

Disciform degeneration of macula

Gliosis

Hemorrhage:
- Juvenile
  - Recurrent

Hole:
- Extramacula
- Macula

Hyaloid bodies or residual edema [17]

Hyperplasia of pigment epithelium

Internal limiting layer:
- Detachment
- Thickening

Macular changes

Oral fibrosis [18]

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17. The terms hyaloid bodies or residual edema refer to the localized eosin-staining foci that occur in the external plexiform layer of the retina in cases of retinopathy associated with nephritis, diabetes and malignant hypertension and in other conditions which produce a stasis in the retina, such as papilledema and similar conditions.

18. The term oral fibrosis is used instead of ring Schwiele.

Retinitis:
- Cachectica
- Following inflammation of anterior segment
- Idiopathic
- Massive
- Metastatic
- Pigmentosa
- Proliferans

Traction membrane [19]

Varicose nerve fibers or cytoid bodies

Sclera

Abscess:
- Metastatic

Compression [20]

Scleritis:
- Actinic
- From necrotic tumor
- From orbital cellulitis
- Idiopathic
  - General
  - Anterior
  - Posterior
- Traumatic

Shrinkage [21]

Senile Changes

Cornea:
- Arcus senilis
- Excrescences of Descemet's membrane

Iris:
- Atrophy of pigment seam
- Sclerosis of sphincter muscle

19. The term traction membrane is used to designate the fibrous tissue that organizes along the anterior hyaloid membrane from exudate or hemorrhage and which frequently produces a detachment of the retina by its contracture.

20. The term compression is used to designate cases in which the sclera is pushed in by orbital lesions.

21. The term shrinkage designates the thickening and contraction of the sclera which takes place in atrophic and phthisic eyes.

Lamina vitrea:
- Excrescences
  - Of choroid
  - Of ciliary body
- Thickening

Retina:
- Peripheral cysts (see *Cysts:* Of retina)

Sclera:
- Calcium (see *Degenerations*)
- Hyalin (see *Degenerations*)

Systemic diseases:
- Arteriosclerosis (see *Systemic Diseases*)

Staphyloma

Ciliary
Corneal
Equatorial
Intercalary
Posterior

Sympathetic Ophthalmia

Following injuries
Following operation
Following tumor
Following ulcer
Idiopathic
Sympathizing eye
Uveal pigment test

Systemic Diseases [22]

Actinomycosis
Amaurotic family idiocy

Arteriosclerosis:
- Retinopathy

Arthritis:
- Uveitis

Chloroma
Cysticercus cellulosae

22. All ocular changes due to a general disease are listed under *Systemic Diseases.*

Deficiency diseases:
- Keratomalacia

Diabetes:
- Cataract
- Edema of pigment epithelium of iris
- Iritis
- Retinopathy

Glanders
Hodgkin's disease
Hurler's disease
Hydrocephalus

Hyperthyroidism:
- Dacryoadenitis
- Myositis

Leprosy

Leukemia:
- Lymphatic
- Myelogenous

Lupus erythematosa disseminata:
- Atrophy of optic nerve

Meningitis

Nephritis and hypertension:
- Papilledema
- Retinopathy

Periarteritis nodosa
Pernicious anemia
Purpura
Septicemia

Syphilis:
- Choroiditis
- Gumma
  - Of choroid
  - Of ciliary body
  - Of iris
  - Of lid
  - Of orbit
- Interstitial keratitis
- Meningitis
- Optic neuritis
- Scleritis

Tabes
Uveitis

Trichiniasis:
Myositis
Toxoplasmic encephalomyelitis

Tuberculosis:
Of choroid
Of ciliary body
Of conjunctiva
Of cornea
Of iris
Of lacrimal gland
Of meninges
Miliary
Of optic nerve
Of orbit
Panophthalmitis or endophthalmitis
Of retina
Of sclera
Xanthomatosis

Tumors [23]

Of caruncle:
Fibromyoma
Nevus
Papilloma

Of choroid:
Carcinoma—metastatic
Hemangioma
Melanoma
Benign
Malignant
Neurofibroma [24]
Retinoblastoma [25]
Sarcoma—metastatic

23. The terminology of tumors of the peripheral nerve structures as employed in this classification is explained in footnotes 24 to 30.

24. Neurofibroma is a tumor of von Recklinghausen's disease which may be a terminal neurofibroma, a sheath neurofibroma, or a plexiform neurofibroma.

25. It will be noted that retinoblastoma is listed not only under tumors of the retina but also under tumors of the optic nerve, of the choroid, etc. In the latter sites it means that the tumor has spread secondarily.

Of ciliary body:
- Adenoma
- Carcinoma
  - Primary
  - Metastatic
- Dictyoma
- Leiomyoma
- Melanoma
  - Benign
  - Malignant
- Neurofibroma [24]

Of conjunctiva:
- Adenoma
- Angioma
  - Hemangioma
  - Lymphangioma
- Dermoid
  - Cyst
  - Tumor
- Dermolipoma
- Epithelioma
  - Basal
  - Squamous
  - Mixed
- Fibroma
- Lipoma
- Lymphosarcoma
- Melanoma
  - Benign
  - Malignant
- Nevus
- Neurofibroma [24]
- Papilloma
- Plasmoma
- Xanthoma

Of cornea:
- Epithelioma

Of iris:
- Carcinoma
  - Primary
  - Metastatic
- Dictyoma

Leiomyoma
Leiomyosarcoma
Melanoma
Benign
Malignant

Of lacrimal apparatus:

Adenoma
Carcinoma
Lymphosarcoma
Mixed tumors

Of lids and brow:

Adenoma
Angioma
Hemangioma
Lymphangioma
Carcinoma
Metastatic
Primary
Epithelioma
Basal
Squamous
Mixed
Of meibomian gland
Of sweat gland
Dermoid
Cyst
Tumor
Fat necrosis
Fibroma
Hematoma
Lipoma
Lymphoma
Melanoma
Malignant
Nevus
Neurofibroma [24]
Neuromyoarterial glomus [26]
Papilloma
Plasmoma
Sarcoma
Teratoma

26. Neuromyoarterial glomus is a tumor involving nerve terminals.

Verruca
Xanthoma
Xeroderma pigmentosa

Of limbus:
Dermoid
Epithelioma
Basal
Squamous
Mixed
Heterotopic tissue
Melanoma
Benign
Malignant
Nevus
Neurofibroma [24]
Teratoma

Of lymph node:
Melanoma
Malignant

Of meninges:
Carcinoma
Metastatic
Meningioma (see *Orbit*)
Sarcoma

Of muscles:
Carcinoma
Metastatic

Of optic nerve:
Carcinoma
Metastatic
Glioma
Melanoma
Benign
Malignant
Meningioma [27]
Retinoblastoma [25]

27. Footnote 25 also explains the presence of meningioma under tumors of the optic nerve. When it is listed under this heading, it refers to cases in which it has extended into the nerve secondarily.

Of orbit:

- Angioma
  - Hemangioma
  - Lymphangioma
- Carcinoma
  - Extension
  - Primary
  - Metastatic
- Dermoid cyst
- Fibroma
- Hematoma
- Lipoma
- Lymphoma
- Lymphosarcoma
- Melanoma
  - Malignant
- Meningioma
- Neurilemoma (neurinoma) [28]
- Neuroblastoma [29]
- Neurofibroma [24]
- Osteoma
- Pseudotumor (see *Orbit:* Orbital granuloma)
- Retinoblastoma [25]
- Sarcoma
  - Fibrosarcoma
  - Leiomyosarcoma
  - Lymphosarcoma
  - Rhabdomyosarcoma
  - Unclassified

Of retina:

- Angiomatosis
- Carcinoma
  - Of pigment epithelium
- Dictyoma
- Pseudotumor [30]
- Retinoblastoma [25]

28. Neurilemoma is a specific nerve sheath tumor (neurinoma, schwannoma, perineural and fibroblastoma).

29. Neuroblastoma is a malignant tumor of the neuroepithelium.

30. The term pseudotumor under tumors of the retina designates those conditions which are confused clinically with retinoblastoma, such as a late metastatic retinitis, the remains of the vascular capsule of the lens and some cases of retinitis proliferans. These cases are also included under the proper headings elsewhere, such as congenital anomalies, inflammations, etc.

Of sclera:

Retinoblastoma [25]

Vascular Changes

Aneurysm between internal carotid and cavernous sinus
Arteriosclerosis (see *Systemic Diseases*)
Occlusion of central retinal vessels
Occlusion of ciliary arteries
Thrombosis of cavernous sinus

Vitreous

Abscess
Asteroid hyalitis
Detachment
Hemophthalmos

SCLEROCORNEAL TREPHINING (ELLIOT'S OPERATION)

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The essential purpose of the sclerocorneal trephine operation described by Elliot in 1909[1] is to provide a subconjunctival fistula through which aqueous humor can escape from the globe into the conjunctiva. Under proper conditions the aqueous humor will be diffused over the eyeball and gradually absorbed into the general circulation under cover of an intact conjunctival epithelium.

Several modifications of Elliot's operation have been devised to overcome certain technical difficulties in the procedure, to make it applicable to the various types of glaucoma or to make it more effective and the result more enduring. Since it was meant to supplant other methods of fistulization, such as those of Lagrange,[2] Herbert,[3] Fergus[4] and others, Elliot advocated its use in all forms of glaucoma.

The classification of glaucoma into congestive or inflammatory, caused by swelling of the ciliary processes, and noncongestive or simple, caused by alteration in the size and position of the lens, is the classification used by Elliot.[5] The distinction between the two conditions lies in the presence or absence of obstruction to the free escape of blood from the eye. The distinction between the two conditions, according to Elliot,[5] is not a radical one. It depends on conditions which at any time may alter and which in doing so will profoundly modify the clinical aspect of the condition.

From the Section on Ophthalmology, the Mayo Clinic.

Read before the Section on Ophthalmology at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Elliot, R. H.: A Preliminary Note on a New Operative Procedure for the Establishment of a Filtering Cicatrix in the Treatment of Glaucoma, Ophthalmoscope **7**:804-806 (Dec.) 1909.

2. Lagrange, F.: Iridectomie et sclérectomie combinées dans le traitement du glaucome chronique; procédé nouveau pour l'établissement de la cicatrice filtrante, Arch. d'opht. **26**:481-496, 1906.

3. Herbert, H.: Operations for Filtering Cicatrices, Ophthalmoscope **6**:483-485 (July) 1908.

4. Fergus, F.: Treatment of Glaucoma by Trephining, Brit. M. J. **2**:983 (Oct. 2) 1909.

5. Elliot, R. H.: Glaucoma: A Textbook for the Student of Ophthalmology, London, H. K. Lewis Co., Ltd., 1918, p. 130.

Additional experience with the Elliot operation has shown that it is much more effective for the chronic simple or noncongestive types of glaucoma than for the congestive type, and most ophthalmic surgeons now hesitate to perform a corneoscleral trephine operation for acute congestive glaucoma. The reason for the lack of satisfactory drainage when Elliot's operation is performed in acute congestive glaucoma is found in the passive congestion of the conjunctiva. The obstruction to free escape of blood prevents absorption of the aqueous humor from the conjunctival tissues. Free escape of the aqueous humor is also interfered with by adhesions of the conjunctiva to the sclera, and these adhesions are likely to become rather dense following inflammation of the conjunctiva caused by disease, injury or antecedent surgical treatment. It is beside the purpose of this paper to argue the merits of the Elliot operation, and I do not intend to defend its selection as the method of choice for any type of glaucoma. That the operation is followed by satisfactory results for chronic simple or noncongestive glaucoma is generally conceded, and in English-speaking countries it is the operation most frequently employed for the condition under consideration.

Successful results may be expected in a high percentage of uncomplicated operations in properly selected cases, but failures have been encountered when conditions for operation seemed favorable. The reasons for failure have been attributed to postoperative inflammatory reactions not clearly explained. The formation of adhesions about the site of trephination blocks the passage of fluid from the anterior chamber, resulting in the formation of a vesicle covered only by a thin layer of conjunctiva; the conjunctival flap becomes thick and fibrous over the site of trephination and closes the fistula; epithelial or uveal tissue grows into and blocks the opening, and the intraocular tension is maintained at a high degree. All these complications may be the result of faulty technic or a poorly performed operation.

Elliot [6] recognized the necessity of having freely movable conjunctival tissues into which the aqueous humor could diffuse. He stated:

> A careful study of a number of cases after operation shows that the actual line of the incision is sometimes tied down on to the sclera; if one makes a flap of little length, it tends to curl in on itself; moreover, if the two ends of the incision reach the cornea, and if the line of union then cicatrizes, it is obvious that the total area left for filtration is very limited.

In his first description of the operation, Elliot advocated the dissection of a large flap extending from the upper fornix to the limbus, including nearly a half of the anterior portion of the globe. The incisions bound-

6. Elliot,[5] p. 449.

ing the flap extended to the limbus on each side of the cornea, ending somewhat above the horizontal meridian. Later, Elliot modified the flap by using a long, curved incision, beginning 8 mm. from the limbus on one side, extending through the upper fornix and ending 8 mm. from the limbus on the opposite side of the cornea in the horizontal meridian. Instead of dissecting up a large flap completely, as he had earlier advocated, Elliot's later modification carried the dissection down to the limbus over the central portion only. Elliot realized that after free dissection of the flap the conjunctiva became so firmly attached to the underlying tissues that cicatricial bands obstructed the free flow of fluid and interfered with drainage from the chamber. Not only would the flap become adherent to the sclera at the line of incision, but throughout the area of the flap the conjunctiva would tend to become firmly adherent, particularly where free dissection had been carried out. It was in order to avoid these cicatricial obstructions to the free flow of aqueous humor that Elliot modified his incision so that there was a nonobstructed region between the limbus and the end of the incision through which the aqueous could pass more freely. His advice to restrict free dissection to the central area of the flap also was based on the same reasoning.

In this later description of the operation, he stated:[7]

> In the upper portion of the dissection we do not need to take up anything but the loose conjunctiva. As we approach the limbus we should work down to the sclera, and should expose the latter bare in the last few millimeters of the wound. At the same time the breadth of the dissection should contract as we approach the cornea, so that when we reach the latter, we only expose just such a breadth of it as we mean to split.

It is obvious from a perusal of Elliot's reports that he realized the importance of avoiding adhesions and contractions in the conjunctival tissues. Nevertheless, he advocated making a large conjunctival flap, entirely disregarding the fact that to make it as he directed would require dissection of the conjunctiva from the capsule throughout the greater extent of the flap.

The making of this flap, as directed by Elliot, was described by Török and Grout[8] as follows:

> A fold of conjunctiva is now grasped with the mouse-tooth forceps about 10 to 12 mm. above the upper limbus and with the curved scissors an incision is made in the conjunctiva. The incision is about 25 to 30 mm. long, runs roughly concentric with the limbus and ends on either side opposite the highest point of the cornea and about 8 mm. to its inner and outer sides. This conjunctival flap is now dissected. It is unnecessary to dissect up the whole area included in the flap, it being more advantageous if we carry our dissection down to the limbus

7. Elliot,[5] p. 452.

8. Török, E., and Grout, G. H.: Surgery of the Eye: A Hand-Book for Students and Practitioners, Philadelphia, Lea & Febiger, 1925, p. 187.

over the central area only. The dissection is done with the forceps and sharp pointed curved scissors. In the upper portion of the dissection we take up only the loose conjunctiva but as we approach the limbus, we should work down to the sclera so that in the last few millimeters it should be bare.

No one ever has satisfactorily explained why a large incision of the conjunctiva was made when only the central portion of the flap was dissected down to the limbus.

Most surgeons have realized the disadvantages of making a large flap as well as a large incision. Wright advocated the making of a relatively short incision in the conjunctiva, concentric with the limbus and about 6 to 7 mm. from it. Von Mende [9] and Dupuy-Dutemps [10] in 1913 recommended loosening of the conjunctiva at the limbus, pulling the flap upward during the operation and afterward fastening it over the wound by a couple of stitches. Bentzen [11] separated the conjunctiva with scissors from the upper limbus. The incision was curved downward, about 10 mm. long, and ended about 2 mm. to the inner and outer sides of the limbus. When the conjunctiva had retracted from the limbus, he used the cataract knife to remove the epithelium and the superficial layer of the cornea in a region about 2 mm. broad, centered over the spot chosen for the site of trephination.

In an article entitled "A New Conjunctival Flap for Trephining Operations," Verhoeff [12] in 1936 advocated division of the conjunctiva at the limbus.

With a Graefe knife the conjunctiva is severed exactly along the limbus for a distance of about 4 mm. With forceps grasping the cut margin of the conjunctiva, the latter is undermined with knife or scissors close to the sclera sufficiently far back to permit exposure of the area to be trephined and also to permit the flap readily to be pulled down well over the cornea. The corneal surface is now denuded of epithelium for a distance of about 2 mm. in front of the selected site. . . . The sclera is trephined, iridectomy performed, and the operation completed by pulling the small conjunctival flap over the opening and tying the suture.

By elevating the conjunctiva at the limbus and dissecting up the conjunctiva over a very small area, the formation of adhesions obstructing the flow of aqueous humor through the conjunctiva is avoided. However, if the dissection is carried upward beyond the attachment of Tenon's capsule "to permit the flap readily to be pulled down well over

9. von Mende, R.: Zur Technik der Elliotschen Trepanation, Klin. Monatsbl. f. Augenh. **51**:354, 1913.

10. Dupuy-Dutemps: Une modification à la technique de la trépanation d'Elliot, Ann. d'ocul. **149**:409-413 (June) 1913.

11. Bentzen, C. F.: On Making the Conjunctival Flap in Elliot's Operation, Acta ophth. **1**:43-45, 1923.

12. Verhoeff, F. H.: A New Conjunctival Flap for Trephining Operations, Am. J. Ophth. **19**:46 (Jan.) 1936.

the cornea," it is likely that the dissection will be carried between the conjunctival epithelium and the capsule in spite of Verhoeff's direction to keep close to the sclera. Consequently, if the flap should be made rather large, more than 5 mm. from the incision, limiting adhesions about the site of the trephine are likely to occur.

The relation of Tenon's capsule to the sclera and the conjunctiva and the difference in elasticity of the capsule and conjunctival tissue constitute the basis for the care needed to provide a satisfactory flap: one which will not impede the diffusion of aqueous humor through the conjunctival tissues. Tenon's capsule is a rather firm, inelastic membrane that covers the eyeball to within 3 mm. of the limbus. Wolff [13] wrote:

> In front of the insertion of the recti tendons the bulbar conjunctiva lies on the anterior portion of Tenon's capsule. Up to a point about 3 mm. from the cornea, the conjunctiva is separated from the capsule of Tenon by loose areolar tissue, and between it and the sclera is the loose episcleral tissue in the anterior portion of Tenon's space. . . . At about 3 mm. from the cornea, the conjunctiva, Tenon's capsule, and sclera become much more closely united. The conjunctiva, like all other mucous membranes, consists of two layers—the epithelium and the substantia propria.

The potential drainage space in the conjunctiva is in the substantia propria between the conjunctival epithelium and Tenon's capsule. Tenon's capsule is nonelastic, as is also the sclera. Consequently, the potential drainage space between the capsule and the sclera is relatively limited, and adhesions between Tenon's capsule and the sclera do not interfere materially with the drainage of aqueous humor. Adhesions between the conjunctival epithelium and Tenon's capsule, as has been noted by Elliot and others, do obstruct the flow of fluid and nullify the function of the trephine operation.

At about 2 to 3 mm. behind the limbus the conjunctiva, Tenon's capsule and the sclera are rather firmly united. Forward from this line only the conjunctiva covers the sclera and the limbus, and it blends with the corneal epithelium 1 to 2 mm. beyond the limbus. It is in this zone between the termination of Tenon's capsule and the termination of the epithelial layer of the conjunctiva, a zone 3 mm. wide over the limbus, that the trephine opening should be made. The opening in the corneosclera is then covered only by conjunctiva, and the aqueous humor diffuses beneath the conjunctival epithelium into the loose areolar conjunctival tissue above the capsule.

Instead of dissecting down a conjunctival flap as described by Elliot, the surgeon may approach the limbus without disturbing the relation between the conjunctiva and the capsule. Consequently,

13. Wolff, E.: The Anatomy of the Eye and Orbit, Including the Central Connections, Development, and Comparative Anatomy of the Visual Apparatus, Philadelphia, P. Blakiston's Son & Co., 1933, p. 103.

delimiting adhesions of the flap to interfere with the diffusion of aqueous humor are not likely to occur. There are two ways in which this may be done, one utilizing a precapsular, the other a subcapsular, approach. In the precapsular approach, as advocated by von Mende, Dupuy-Dutemps, Bentzen and Verhoeff, the conjunctiva may be divided anteriorly to the site selected for trephine opening and the conjunctiva pulled over the hole. Elliot's objection to this procedure was that as a result of it the trephine opening is so close to the incision that it is exposed to infection. Elliot advocated the making of a large flap, principally to safeguard against infection of the eye. Elliot called attention to the desirability of having the trephine opening situated as far as possible from the breach in the conjunctiva, thereby avoiding infection and the downgrowth of epithelium through the trephine opening. Verhoeff commented on this presumption by expressing the following opinion:

> In preparing the usual conjunctival flap, the conjunctiva is dissected up freely around and behind the site for the fistula. As a result, the conjunctiva often becomes firmly fused with the sclera, filtration thus suffers interference, and leads to a marked vesicular condition and danger of late infection.

It is obvious that the ideal method of approach would avoid both of these objections. Although infections occurring through the intact conjunctiva are extremely rare, an incision through the conjunctiva, made at some distance from the trephine opening, would tend to lessen the susceptibility to infection and the downgrowth of epithelium into the fistula. Also, avoidance of trauma to the conjunctiva would obviate the formation of adhesions and the development of a thin conjunctival bleb over the site of the trephine opening. A subcapsular approach to the limbus for trephining can be made without disturbing the relation between conjunctiva and Tenon's capsule, and at the same time the break in the conjunctiva lies at a sufficient distance from the site of the trephine opening so that the eye is not exposed to infection.

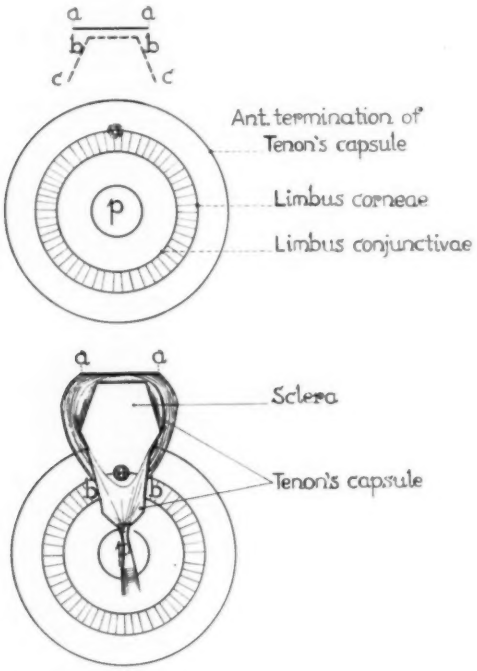
TECHNIC OF AUTHOR'S OPERATION

The operation for noncongestive glaucoma which I have used for more than five years is performed in the following manner:

Anesthesia is provided by the instillation of a 4 per cent solution of cocaine hydrochloride and the subconjunctival injection of a 2 per cent solution of procaine hydrochloride. The conjunctival tissues are grasped by a fixation forceps over the insertion of the superior rectus tendon, and with scissors a linear cut is made 8 mm. from and concentric with the limbus. The incision is about 12 mm. in length. The conjunctiva is then released, and the fixation forceps is introduced through the incision, and Tenon's capsule, which is easily recognized, is grasped and incised with the scissors in line with the incision in the conjunctiva. The forward lip of the capsule is grasped by the forceps, and the blunt tip of the scissors is introduced beneath the capsule; by blunt dissection the capsule is

separated from the sclera. To turn the capsule forward, two wing cuts may be made in the capsule toward the limbus on either side of the forceps. By retaining the tongue of the capsule thus made and pulling it forward, the line of its attachment to the sclera is easily discernible 3 mm. behind the limbus. This line of attachment is carefully opened by the blunt point of the scissors and separated for a distance of about 5 mm. Forward traction on the capsule flap exposes the corneoscleral junction over an area large enough to receive the trephine. The conjunctiva, still attached to the capsular flap, lies forward on the cornea, untouched by any instrument, as shown in the accompanying illustration.

Before the trephine is applied, hemorrhage should be controlled and the site of trephination should be cleared of conjunctival tissue. Care must be taken at this



The approach to the sclerocorneal limbus is made through a small incision in the conjunctiva, *a-a*, and Tenon's capsule, *b-b*, remote from the site of trephination, and the relation between capsule and conjunctival epithelium is not disturbed. The trephine opening, *d*, is not exposed to infection, and adhesions between the conjunctival epithelium and Tenon's capsule are avoided. Wing cuts in Tenon's capsule are indicated by *bc-bc*.

point not to perforate the conjunctiva. The trephine is applied to the corneoscleral junction, and a through-and-through cut is made perpendicular to the surface of the eyeball. When the button is removed the iris will bulge into the trephine opening, and iridotomy may be done. With sharp-pointed iris scissors a single cut is made through the iris as close to the scleral margin of the trephine opening as possible. This results in iridotomy at the basilar portion of the iris. As soon as the iris is cut, aqueous humor escapes, and the iris falls back into the chamber.

A few gentle strokes with an iris replacer over the trephine opening will help to make the iris fall back into its normal position. It is not necessary or desirable to introduce any instrument into the eye through the trephine opening. In uncomplicated cases the iris should not be grasped with forceps. If the iris does not readily present itself on removal of the button, it may be made to bulge into the wound by gentle pressure on the cornea with the forceps that holds the capsular flap. The capsular flap should then be released and stroked back into position and left without sutures. The conjunctiva will resume its normal position, and the edges of incision may be held together by a single suture. A drop of a 1 per cent solution of atropine is instilled, the lids are closed and a dressing is applied.

The reaction following this operation is gratifyingly slight, and the diffusion of aqueous humor through the uninjured conjunctival tissue is not impeded by formation of adhesions, since the only adherent scar is situated 8 mm. above the limbus. The breach in the conjunctiva is far enough from the trephine opening to prevent direct infection. Thus, the two most troublesome complications of the trephine operation are either avoided entirely or reduced to a minimum.

Splitting of the cornea, as advocated by Elliot but thought to be unnecessary by others, is not done. It was Elliot's contention that the cornea should be divided to enable the surgeon to place the trephine as far forward as possible. The necessity of splitting the cornea is not obvious, and I have abandoned the practice. In one particular manner a split cornea is of great help: It forms a shoulder against which the trephine may rest to prevent it from "walking" or sliding from the intended place of application during the first few turns of the trephine. This advantage, however, applies only to the hand-operated instrument and is not needed when the automatic trephine is used. Distinct pressure is required to cut through the cornea with the hand-operated trephine, but with the automatic trephine no appreciable pressure is applied. For more than two years I have used the Green trephine on which an electric motor has been mounted. The advantage in the utilization of this instrument is obvious, as the speed and the power of the blade of the trephine can be regulated to suit the needs or the desire of the surgeon. It runs true, without vibration, and cuts with a minimum of pressure. Any desired angle may be used to cut the corneosclera, so that the button of tissue may be removed totally or partially cut so as to form a hinged flap. Splitting of the cornea can be easily accomplished through the breach in the attachment of the capsule, as I have set forth. It is a detail that is optional with the surgeon. Whereas there is no advantage in splitting the cornea if the electrically driven trephine is used, neither is there a disadvantage in such a procedure. The size of trephine to be employed also is optional. It is my practice to use a blade of 1.25 mm. diameter, although a larger blade may be used, or two or more trephinations may be made contiguously to provide a greater filtration scar.

The subcapsular approach to the corneoscleral junction for purposes of trephination provides easy access to the desired place with a minimum of trauma to the conjunctival tissues through which the diffused aqueous humor must pass freely if satisfactory reduction in tension is to be obtained. Consequently, the conjunctival epithelium is not bound down to the sclera. Sclerocapsular adhesions are not important because the potential drainage space between the capsule and the sclera is negligible.

In making the flap, the conjunctiva is not grasped by the forceps after the first incision is made. It is merely pushed forward by the forceps that hold the capsular flap or by a cotton wound applicator, so that there is little danger of tearing or "buttonholing" the conjunctiva at the limbus.

CONCLUSION

This modification of the Elliot operation as described herein provides safety from infection and obviates constriction of the flap and formation of a vesicle over the fistula. It adds much to the success of the operation.

ABSTRACT OF DISCUSSION

Dr. Algernon B. Reese, New York: Dr. Benedict discusses the best method of dissecting the conjunctival flap in performing the trephine operation in order to assure a diffuse, generous subconjunctival filtration of aqueous humor. He wishes thus to avoid the small localized, elevated, thinly covered, filtering bleb which is confined to the region just over the trephine opening, or the flat conjunctival bed with no filtration, both these conditions being due to conjunctival adhesions resulting from improperly made flaps. He claims that the space between Tenon's capsule and the sclera is a confined, limited one, but that the space between the conjunctiva and Tenon's capsule is potentially large and thus the desirable one for filtration. His dissection, therefore, is not subconjunctival but subcapsular, in order to avoid adhesions between the conjunctiva and the capsule. This is carried down to within 3 mm. of the limbus, where Tenon's capsule ends, and from this point to the limbus the conjunctiva is dissected from the underlying sclera just sufficiently to reach the limbus over a wide enough area to permit the placing of the trephine blade.

In order to identify better the layers involved in this dissection, my colleagues and I give a large subconjunctival and subcapsular injection of procaine hydrochloride. This separates the layers and makes the planes of cleavage quite obvious. Also, in order to prevent the flap from gravitating downward and becoming redundant over the cornea, we anchor the central conjunctival suture to the fascia of the superior rectus muscle.

Dr. Benedict has brought up a very important, and perhaps somewhat neglected, feature of the trephine operation, and I am grateful to him for making me more flap conscious.

There is one feature of Dr. Benedict's technic with which I do not agree. This is his practice of never shelving the cornea. This is unnecessary in most instances because the limbus above normally extends approximately 2 mm. onto the cornea. In some instances it extends 3 mm. or more. At other times, however, the limbus above extends only 1 mm. or less, and rarely not at all. In these cases it ends at a site corresponding to or near the scleral spur, and in order to have the trephine opening entirely in the anterior chamber it is necessary to shelve or split the cornea.

Furthermore, if a trephine operation is done anywhere but in the vertical meridian above, that is, between 11 and 1 o'clock, shelving the cornea is necessary, because elsewhere the limbus normally extends only about 1 mm. or less onto the cornea.

In chronic glaucoma of any great duration the limbus extends farther than in nonglaucomatous conditions because of the tendency for vascularized fibrous tissue to interpose itself between the epithelium and Bowman's membrane (pannus glaucomatosa). This fact would seem to make corneal shelving unnecessary. However, in cases of glaucoma of long standing in which peripheral synechia are present, the trephine opening should be placed further within the cornea, in order to have the opening enter the anterior chamber beyond the synechiae, instead of through the synechia into the posterior chamber. In such cases shelving would be required. I do not believe, therefore, that one can have an ironclad rule for this procedure.

Dr. Manuel Uribe Troncoso, New York: The statistics of different surgeons show great variations in the results of trephining operations for the treatment of glaucoma. This undoubtedly depends, first, on the stage of the disease in which the operation is done and, second, on the reaction of the eye to operative trauma and the presence of infection.

The stage of glaucoma at the time trephining is performed is of great importance. The results are better when the operation is done in the early periods of chronic noncongestive glaucoma, when there is little hypertension, the field of vision is not greatly impaired and the angle of the anterior chamber is open or only partially closed by peripheral synechia. When there is an open angle the trephine hole falls in front of the root of the iris and there is less tendency to complications and cicatricial closure of the aperture. But when the operation is done in an advanced stage and there is already a wide peripheral synechia, the trephine may cut through the synechia and even penetrate the posterior chamber. The iridectomy usually done before trephining fails to detach the posterior synechia. The ciliary processes are drawn forward and become closer to the scleral opening. In these conditions several complications occur which can be detected only by the use of gonioscopy.

It is strange that the surgeons before and after an operation performed in the corneal limbus ignore what is happening in the inner side of the structures involved. When gonioscopy is performed before trephining, the surgeon obtains reliable information about the condition of the angle and is able to detect the existence of a partial or complete peripheral synechia. In this way he may choose the best place for his operation and foresee to a certain extent the operative results.

After the operation is done, examination shows whether the technic was correct and whether any complications are present. In a former paper (Troncoso, M. U., and Reese, A. B.: Gonioscopic Findings After Elliott Operation, *Tr. Ophth. Soc. U. Kingdom* **53:** 366-391, 1933; *Am. J. Ophth.* **18:** 103-119 [Feb.] 1935) these complications have been described in detail. I shall now confine myself to mention of the following:

1. Incarceration of the pillars, and even of the whole base of the coloboma, into the scleral scar.

2. Incarceration of shreds or bands of the uveal layer of the iris from the base of the coloboma into the scleral scar.

3. Incarceration of the ciliary processes into the scar. Sometimes one or two processes, at other times the whole row, is drawn forward into the anterior chamber through the aperture of the coloboma and becomes attached to the scar. This complication is more frequent when the processes are swollen and pushed forward and become closer to the scleral hole.

4. Production of exudates which may give rise not only to posterior synechia, but also when extensive to strands or membranes which bind the edges and base of the coloboma to the scleral scar and even may entirely obliterate the new opening in the iris and the scleral aperture. The inflammation may be so active that in some cases the processes are buried in a mass of exudates which becomes adherent to the operative scar.

An apparently good result of the trephining may change later to failure, owing to some of these complications.

I have seen many trephine operations done one after another, as many as five on the same eye, and all unsuccessful, due to the condition of the inner structures and to mild infection, which closes the scleral hole soon after it is made.

It is to be hoped that in the future surgeons will operate in their cases of glaucoma at as early a period as possible, and that they will make the examination of the angle of the anterior chamber both before and after operation to locate before the procedure the better place for the opening and to detect afterward the condition of the coloboma and any existing complications at the angle.

Dr. H. Maxwell Langdon, Philadelphia: The basic idea of Dr. Benedict's thesis is the obtaining of a filtering flap. Even if all surgeons adopt his interesting and, I am sure, useful technic, I have no doubt that some will be unsuccessful at times. It will happen that the flap closes down. Dr. J. A. McMillan, of Montreal, at a meeting of the American Ophthalmological Society a year ago, made a valuable suggestion, namely, that air be injected into the anterior chamber and allowed gradually to filter out, thus preventing early adhesions. I have tried this procedure on 2 occasions; I might have had success without it, but I was sure of good results with it.

I have had 2 patients who over a term of five or six years have given me a great deal of trouble with recurrent adhesions of the flap to the underlying tissues. In 1 case I have had to raise the flap twice, and in the other three times. One of the patients returned last autumn

with an adhesion and the flap flattened out. I thought I would raise the flap and inject air into the anterior chamber through the trephine hole, which I was sure was open. Each time I had lifted the flap before the aqueous humor had immediately welled out. Instead of raising the flap, however, I simply injected air under the flap and placed the needle into the anterior chamber through the trephine hole. One could see the air bubbles in the anterior chamber. I filled it well, and the patient has gone longer since the operation without a recurrence and without any trouble than at any preceding time. It has only been eight months, so she may have difficulty later; but the technic is one which I suggest to those who get in trouble in spite of Dr. Benedict's methods.

Dr. Benjamin Rones, Washington, D. C.: For many years one of the most persistent advocates of the trephine operation in this country was Dr. Wilmer. He also encountered these complications and tried ingenious variations in an attempt to obviate them.

His first problem was the minimization of latent infections, and he attempted to accomplish this by the use of a Tenon's capsule graft over the trephine opening. He soon found the capsule was just as liable to proliferate as conjunctiva and subconjunctival tissue; as a matter of fact, as far as he could see, it was a good way of plugging up a nice trephine opening; so this procedure was soon given up.

Then, in an attempt to prevent the delimiting fibrosis that Dr. Benedict stresses, Dr. Wilmer also had an ingenious operation in which he used a discission knife on the subconjunctiva, attempting to cut away this scar tissue. This, again, seemed to work in some cases, but in the majority of instances the same sort of fibrosis would occur again.

My associates and I tried various kinds of flaps, bringing them down low, or closer to the limbus, and all we could determine was that the scar formed there was denser and one could raise the flap and place it farther back.

We in the southern portion of the country, probably unlike Dr. Benedict, find that the person's pigmentations plays some role in the amount of scar tissue formed. In other words, if one observes carefully the failure due to the fibrosis that occurs in these flaps, one will probably notice that it is frequent in darkly pigmented persons. It will be found that the percentage of failures among Negroes is infinitely greater than that among blue-eyed, lightly pigmented white persons.

Dr. Friedenwald has succeeded to a great degree in minimizing this formation of scar tissue by the use of beta ray radiation. I am not quite sure how extensive his experience has been to date, but last year it was rather favorable; it seemed to me a much more important method of minimizing the danger than any perfection of technic that may be advocated, and I feel it offers the best possibility of managing this particular complication.

Dr. William L. Benedict, Rochester, Minn.: I agree with Dr. Reese that splitting of the cornea may be advisable. Dr. Elliot advocated it in order to get the trephine as far forward as possible in the cornea; however, as I stated, with the mechanical trephine one has less difficulty

in getting forward than with the hand-operated trephine. Construction of the flap as I have described permits splitting the cornea perfectly well. In former years I did split the cornea. In order to get down to the area in the cornea where trephining is effective, it may be necessary, because of peripheral synechia, to go farther forward in some cases than in others, but I bear in mind then that probably some other operation than the trephination would have been advisable.

I am neither defending nor advocating the trephine operation. I am merely stating that in performing this operation certain failures may be avoided by making a flap that does not permit adhesions to form so easily between the conjunctival epithelium and the capsule.

Dr. Troncoso's discussion also concerned the question whether or not a trephine operation is indicated in a particular case. Of course, if the angle of the anterior chamber has moved so far forward that a trephine cannot well get into the anterior chamber, one should probably choose some other form of operation.

Furthermore, if the trephine is not forward of the adhesions between the iris and the posterior surface of the cornea, a buttonhole may be made through the iris. Even though it does not bulge into the wound, a cut in the iris may still be made, for it is known that in many instances a wound in the iris does not heal.

In regard to Dr. Langdon's suggestion of injecting air into the anterior chamber: I have had no experience with such a procedure, but I have, of course, no objection to it.

The necessity of cutting away adhesions is apparent to all who have had adherent flaps; to obviate these adhesions is the object of the procedure that I have described.

I should like to know whether the flap that was used by Dr. Wilmer was entirely in the conjunctiva, in what I call the drainage area. From personal communications, I have reason to believe that Dr. Wilmer used a very large flap, such as was described by Elliot. Such a flap was started with only the epithelium of the conjunctiva, but as he approached the termination of Tenon's capsule on the sclera, about 2 mm. above the corneoscleral junction, he descended deeper into the tissues of the conjunctiva. If that is correct, then the manner in which the flap was made would tend to permit formation of adhesions, whereas if the dissections had been entirely subcapsular, adhesions probably would not have occurred.

I, too, have found, as Dr. Rones has suggested, that it is more difficult to prevent adhesions in Negroes.

I have had no experience with beta ray radiation.

WHAT IS THE MINIMUM ROUTINE EXAMINATION OF MUSCLES?

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With the varying opinions as to the necessity of a routine examination of the muscles and with an almost equal variance in the choice of tests to be used, it is difficult to make a choice of procedure. There is, too, a hazy idea of what the tests are made for, why the tests vary in the amounts of deviation and what the results really mean.

The many diagnoses of exophoria, esophoria and hyperphoria, as such, without any further classification, seem to be evident proof that the underlying reasons for these phorias and tropias are not too clearly understood.

In postgraduate teaching and in various examinations I have found such a lack of definite understanding or purpose that a description of a well tested routine and the reasons for such would not be out of place.

A routine examination should include the following points, each to be considered in detail:

(*a*) History, including observations by the examiner
(*b*) Vision
(*c*) Refraction
(*d*) Accommodation
(*e*) Deviation for distance
(*f*) Deviation for near vision
(*g*) Deviation in the six cardinal fields
(*h*) Convergence near point.

The determination of these points are all that is necessary to a diagnosis. Tests may be made to confirm or to check the results of the routine tests, and when a diagnosis is made additional tests may be used for further evidence on a definite point.

POINTS OF ROUTINE EXAMINATION

History.—The present complaint is described, and any past history bearing on the case and any hereditary probabilities are questioned. One should observe any abnormal position of the head or other characteristics without mentioning them until later.

Space should be left to add any additional history brought out later, especially intimate points which the findings might prove necessary but which are too intimate to ask about routinely.

Vision.—The vision must be taken, not only to determine the acuity but to note other important points indicating astigmatism or accommodative strain. When there is a paretic muscle, the head should be turned away from the field of action of the paretic muscle. If this is not done the nystagmoid action caused by the paretic muscle may make the vision seem much less than it actually is. In a recent case vision was reported as 5/200, but with the head turned away from the field of the paretic muscle, the vision was 20/40 without glasses.

If the vision is not as good as 20/30 or cannot be improved to 20/30 or better by lenses, the tests of the accommodation can only be approximated.

Refraction.—It is necessary next by some method to determine the approximate degree of ametropia, improving the vision to 20/20 if possible but at least to 20/30 +. This may be possible for children under 6 years of age, but even here the muscle balance should be determined before any cycloplegic is given. A precycloplegic test of the ametropia is made so that the test of the accommodation may be more nearly accurate and so that one may determine later whether correction of the ametropia changes the muscle balance. Such a change is a common finding. An exophoria is often increased by plus lenses and reduced by minus lenses, or an esophoria may be increased by minus lenses and decreased by plus lenses. A child of 5 years had a divergent squint estimated at 70 to 80 centrads. Under atropine, a + 8.50 D. sph. ⌒ + 0.50 D. cyl. was prescribed for the right eye and a + 9.50 D. sph. ⌒ + 0.50 D. cyl. for the left eye. A 2.5 D. sph. was taken off, and the child now has for distance and near vision an exophoria of 40 centrads alternating with an exotropia somewhat higher. His convergence near point has improved and is absolute part of the time. These differences with and without glasses should be noted and considered in the final analysis. If lenses have but little or no effect on a muscle imbalance, one is suspicious at once of an individual muscle anomaly rather than of an accommodative anomaly, or possibly there may be an anomaly of the systemic type. Likewise, if atropine has no effect on the muscle imbalance, little if any effect is expected from lenses.

Accommodation.—The near point of accommodation should then be taken. Next to a trial case, the most important instrument is a Prince rule. The near point of accommodation should be taken in every case with the glasses on or allowed for. When the vision is less than 20/30, the accommodation should be estimated by Jaeger's test type.

The test object chosen by Duane after much experimenting was an engraved line 3 by 0.3 mm. on an unglazed card.

Each eye should be tested separately with the ametropia corrected. It is often better to follow this by a test with both eyes uncovered, when the accommodation may be from 0.50 to 2.00 D. better, than with either eye alone.

An inequality in the accommodation of the eyes may be due to a difference in visual acuity or to an error in the manifest refraction or to a lesser degree of accommodation in one eye.

Subnormal accommodation is commonly seen when the accommodation is tested routinely. It is usually present in a convergence insufficiency of the systemic type, in toxic conditions, in most debilitating disease, in excessive or perverted sexual functions or in any condition that makes the patient below par. A young man of 27 complained of much burning and smarting of the eyes on near work. The degree of ametropia was low, and the accommodation near point was very remote. A + 1.50 D. sphere was added, which brought the punctum proximum to 4 D. A trial of one week with + 1.50 D. sphere as grab fronts relieved his symptoms entirely, and this was added in the form of bifocal lenses. These have been worn for over four years, with still no return of symptoms. A further questioning into his history brought out the story of a severe streptococcic infection three years before. No doubt he had been struggling with a subnormal accommodation since that time. Many such cases could be cited.

Much sympathy is lost on the myope, it being assumed that because he does not have to accommodate his ciliary muscle is atrophic, making normal accommodation impossible. I find as high an average accommodation in a person with myopia of less than 5 D. as in the hyperope, and the punctum proximum is normal for many persons with myopia of from 5 to 10 D. The constant use of the Prince rule will bring out many interesting and important details that are frequently overlooked. In obscure cases in which marked asthenopia is present, a subnormal accommodation frequently is the cause of the symptoms. When the Prince rule is used routinely, one frequently finds a patient of 35 to 40 using his eyes as the average patient of 50 to 55 and many persons of 45 to 55 accommodating as well as the average patient of 35 to 40.

The advice I gave to a class of prepresbyopic ophthalmologists was not to ask the age of a patient before testing the accommodation and thus avoid being prejudiced regarding the age. I believe it was a French ophthalmologist who said years ago: "The younger the ophthalmologist, the stronger the presbyopic correction given." There is frequent proof of this.

Deviations for Distance, Near Vision and in the Six Cardinal Fields.—It is necessary to consider what is important in a routine test and why.

The normal physiologic acts of the extraocular muscles should be considered first. These are, first, the action of each individual muscle in its effects of lateral rotation, elevation, depression and torsion; second, the action in associated movements; third, the disjunctive act of convergence which takes place within 20 feet (6 meters); fourth, the disjunctive act of divergence which normally controls the fixation at 20 feet and beyond, and fifth and sixth, the acts of sursumvergence and rotation respectively.

With these points in mind, the practical solution of a large majority of muscle problems is rendered simple, while the more complex ones, considered in the same way, are often resolved into their simplest components and so diagnosed.

Phorias and tropias are often spoken of as definite entities instead of as being the result of some abnormal function. For example, an exophoria or exotropia is found for distance. What is the cause? An exophoria or an exotropia could be produced by a paretic internal rectus muscle or by an overacting external rectus muscle. It could also be produced by an excessive divergence action (divergence excess). Even then, an exophoria has not been explained until the test is made for the near point also.

If the exophoria or exotropia increases when the patient looks to the right, it is due to a weak left internal rectus muscle, and if it increases when he looks to the left, it is due to a weak right internal rectus muscle. If, however, it does not increase when he looks to the right or left, it is not due to a paretic muscle, since a deviation due to a paretic muscle must increase in the field of the paretic muscle. There are few exceptions to this rule. The exophoria must then be due to an excessive divergence or to an underacting convergence function. If it is more abnormal for distance, one is probably dealing with a divergence excess; if it is more marked for near vision, the converging function is less than normal, or a convergence insufficiency or paralysis is present. Therefore, to analyze an exophoria or exotropia, the deviation must be measured for distance and near vision and also when the patient looks to the right and to the left.

An esophoria is found for distance. Again is it more for distance or near vision or when the patient looks to the right or to the left? If it increases when he looks to the right, the right external rectus muscle is paretic, and if it increases when he looks to the left, the left external rectus muscle is paretic. If the esophoria increases when he looks both to the right and to the left, both external rectus muscles are paretic. However, if the deviation is not increased in lateral rotations, one must determine whether the crossing of the visual axes is more marked for distance or for near vision. If the deviation is greater for distance, there is an underaction of the diverging function, while the

external rectus muscles per se are normal. If it is greater for near vision, there is an overaction of the convergence function or a convergence excess.

A right hyperphoria or tropia is found in the primary position (eyes front). Is this an anomaly of sursumvergence or is it due to paresis of one or both of the depressors of the right eye, thus letting the eye rise higher? An overaction of one of the elevators of the right eye could pull the eye too high. Again, the right eye may be higher than the left because the left eye is not high enough. Paresis of either elevator of the left eye would let this eye down, or an overaction of either depressor could pull the eye down too far. Hence, it will be seen that no diagnosis can be made without a measure of the deviation for distance, near vision and in the six cardinal fields. For convenience, the measurement in the six cardinal fields is made by a screen test at about 33 cm., and while at this distance the act of convergence may vary the findings from what they would be at 20 feet, still the measurement is relatively the same and the diagnosis is made on the relation of the findings in the six cardinal positions as well as on the relation between the amounts for distance and near vision in the primary position.

Convergence Near Point.—The power of convergence should be determined carefully. This may be done by the meter angle as described in most textbooks or by having the patient look at an approaching object, the examiner noting when one eye gives up fixing and diverges. The character of fixation should also be observed, i. e., whether binocular fixation is held with ease or with difficulty. The latter method was advocated and practiced by Duane. The patient is told to fix a small object which is made to approach the eye. The examiner should train himself to note the point at which one eye gives up fixation. This measured from the glasses or trial frame placed at the anterior focal point is called the proximal convergence point. For purposes of more mathematical accuracy, Duane chose to take the measurement from the center of rotation of the eyes, which is an almost constant point. A base line is drawn from the center of rotation of one eye to that of the other. Since the center of rotation is 11.5 mm. behind the cornea and the anterior focal point is 13.5 mm. in front of the cornea, the distance between these two points is 25 mm. This amount is added to the proximal convergence point and termed the proximal convergence point from the base line.

An absolute proximal convergence point from the base line is when both eyes fix until at a certain point one eye diverges. This point is usually spoken of only as the proximal convergence point. The convergence near point is called relative when in an actual tropia any

attempt to fix with the squinting eye is given up. This is an important observation when deciding the choice of operation for either convergent or divergent squints.

APPLICATION OF TESTS

The purpose of all tests in measuring the amount of deviation is to break up the desire to fuse. That some tests do this better than others is the experience of all doing muscle work. For many patients the desire to fuse dissimilar images is so strong that tests based on dissimilar images are useless, while for many others they are very accurate. Among such tests are the Maddox rod, Cobalt, red glass and Maddox wing tests.

Other tests depend on the prismatic displacement of the object to be fixed or on a fusing of double vision by the use of prisms. The object is usually a light placed at 20 feet for the distance test. The phorometer is one of the best known instruments for measuring deviations, but the equilibrium, the double prism and other tests may be used. These, too, are at times dependable and accurate, while in other cases they cannot be depended on because of their variations in their ability to break up fusion. The Maddox wing test for either distance or near vision has often wide variations.

All tests so far mentioned depend on binocular vision with ability to fuse, so are useless in the presence of suppression and in most cases of amblyopia. In amblyopia and suppression, a test depending on the corneal reflex, as the perimeter or Hirschberg test, may be used.

It is also impossible to examine children accurately by any of the tests mentioned with the exception of the Hirschberg test.

The screen, or cover, test is the one test that can be used for all patients of any age if each eye separately has the ability to fix the test object. Hence in central scotoma with eccentric fixation the screen test is inapplicable, and one must use the perimeter or Hirschberg test.

Except in such cases, the screen test has a general application superior to any other test, and when its use is mastered and the amount of deviation measured by a prism the test is most accurate. For testing of slight degrees of phorias, especially hyperphorias, the screen-Maddox rod test is most accurate—much more dependable than the Maddox rod test alone. The cover test alone, by keeping one eye covered throughout the test, even when changing a prism for measurement, becomes more accurate than the usual screen method. I am partial to the screen-Maddox rod test for measuring low degrees of vertical phorias. The rod should be placed first before one eye and then before the other to get the full value of the test.

In some cases the amount and kind of hyperphoria will be the same with the Maddox rod before either eye. In other cases the hyperphoria will be of the same variety but will measure more when the rod is

before one eye than when it is before the other. The eye having the lesser amount of hyperphoria is usually the paretic eye, showing primary deviation, while the eye having the greater hyperphoria is the non-paretic eye, with a secondary deviation.

It is not uncommon when the rod is before the right eye to have a right hyperphoria and when it is before the left eye to have a left hyperphoria.

By measuring the amounts of hyperphoria in the upper and lower corners in cases of double hyperphoria paresis of the same muscle of each eye will practically always be found. The superior rectus muscles are most commonly paretic, but both inferior rectus muscles, superior oblique or inferior oblique muscles will give the same findings, and the frequency with which they are paretic is in the order named.

I am willing to admit that if the screen-Maddox rod test breaks up the fusion better than any test before mentioned, the prolonged occlusion test of Dr. F. W. Marlow will break it up still more completely. Whether an increase of an exophoria is actually caused by prolonged occlusion or whether the exophoria present is more thoroughly brought out is open to discussion. Marlow, who has had the most experience with the test, claims that only latent exophoria is revealed. Others, from theory rather than practical experience, claim an actual increase of an exophoria.

My first objection to the prolonged occlusion test is the inconvenience to the patient, especially when the screen and the screen-Maddox rod tests give such satisfactory diagnoses. My second, and main, objection is that for several patients a proximal convergence point from the base line which was remote and not held too well but in which both eyes were still able to fix was changed by prolonged occlusion test to an exotropia with only a relative proximal convergence point.

These tests have been treated rather at length to emphasize the variations that are so frequently found and which may be so confusing.

My routine procedure after measuring the accommodation follows:

1. Determination of the deviation for distance with the screen test, measured by a prism (often checked by the Maddox rod and the screen-Maddox rod tests for comparison).
2. Determination of the deviation for near vision (screen test).
3. Determination of the convergence near point (proximal convergence point from the base line), made here for convenience and celerity.
4. Determination of the deviation in the six cardinal fields (measured by prism). The object to be fixed is held at about 33 cm.
5. Use of the screen comitance test in the six cardinal fields if test 4 shows paresis of any muscle. This is done first with one eye fixing, then the other, the examiner watching both eyes for any underaction of the paretic muscle, secondary deviation of the associate muscle or secondary contracture of the direct antagonist.

A prism divergence test (abduction test) and prism convergence test (adduction test) are never necessary to make a diagnosis and are not used routinely by me. However, the younger men are advised to use them until they have formed their own opinions.

If the routine test has shown a divergence insufficiency or divergence excess, then a prism divergence (abduction) test for distance may be interesting while not necessary.

In convergence insufficiency, a prism convergence (adduction) test is usually made for near vision, but in convergence excess the test is rarely used, as it is unnecessary and is apt to accentuate the esophoria for near vision without giving any information and gives real discomfort to the patient.

A diplopia test taken on the tangent curtain is not made routinely. It is purely a subjective test and cannot be relied on for children under 7 or when the paralysis is marked. The test cannot be used in cases of suppression of the amblyopic eye or in alternate fixation with suppression.

It is advisable to make a diplopia test and to chart the findings in court cases, compensation cases or consultation cases in which it might be easer to make the test than to explain why it was not made. The younger man is advised to make this test in all such cases or when the other tests used may need confirmation.

It has already been stated that the deviations in any patient may vary, depending on how completely the fusion is broken up. Many patients showing an exophoria by the cover test will have an esophoria when tested by the Maddox rod, the phorometer or some other method. Likewise, an esophoria is generally less by the cover test than by the tests depending on binocular fixation.

The amount of deviation had little if any bearing on whether the imbalance is a phoria or tropia. I have seen an exophoria of 55 centrads for distance and near vision, with a proximal convergence point of 60 mm. from the base line. An esophoria of 35 centrads and a hyperphoria of 35 centrads have been observed. These are extreme cases, but amounts somewhat less are frequently seen. On the other hand, a low amount of deviation may be an actual tropia; hence each patient should be tested to determine whether it is a phoria or tropia, irrespective of the amount of deviation. This observation can be made along with the screen test and does not consume any additional time.

Since the cover test is a purely objective test, one must train oneself to observe carefully. Of prime importance is a well diffused light of the indirect type—one which will not be too bright for the patient to look toward but will still enable the examiner to see all ocular movements.

When the whole responsibility rests on the examiner, he naturally becomes more alert and self reliant.

There are certain accepted norms, but these are to be taken with caution. As before stated, there may be a high degree of muscle imbalance by measurement; still the symptoms may be absent or negligible. On the other hand, the muscle imbalance may be well within the normal and still be the cause of marked asthenopia, headache and other symptoms. It is necessary, therefore, to examine the muscle balance carefully and to get any further history that might bear on the case. With these in mind, consider the ametropia and the accommodation, and with this evidence decide what are the most probable factors producing the symptoms. When so considered the treatment can be at least intelligently approached.

NORMS

The norms of accommodation are as follows:

For Distance.—An exophoria or esophoria of 1 to 2 centrads is generally considered normal. A hyperphoria of 1 centrad may be normal if it does not increase in the upper or lower corners.

For Near Vision.—An exophoria from 1 to 7 centrads is normal. Any esophoria for near vision may be the cause of symptoms; hence no esophoria for near vision is considered normal or at least is under suspicion.

Neither exophoria or esophoria should increase when the patient looks to the right or to the left. No hyperphoria should increase when he looks in any of the six cardinal fields. These findings are based on the screen test. When the Maddox rod test or similar tests are used, the exophoria for both distance and near vision are frequently less than when taken by the screen test. A low degree of exophoria by the screen test may be, and often is, an esophoria by other tests. Likewise, an esophoria for distance and near vision is usually less by the screen test than by the other tests that do not as completely break up fusion.

The convergence near point should be between 45 and 90 mm. from the base line. For children with a narrow interpupillary distance the convergence near point may be abnormal at 40 mm. from the base line, while for adults, especially those with a wide interpupillary distance, 100 mm. may be normal. Even when it is considerably more remote it may not produce symptoms. When resolved to degrees of arc by the formula, $\frac{\text{½ Pd.} \times 50}{\text{PcB.}} + 3 =$ convergence in degrees, the normal is from 35 to 55 degrees.

Prism divergence (abduction test) is normal from 3 to 9 centrads, with the majority from 4 to 7 centrads.

Prism convergence (adduction test) is normal from 10 up to 70 centrads or more. There is a definite trick about overcoming prism, base out, and many persons can increase the amount rapidly to high

figures, 60 to 90 centrads, while in prism divergence the amount of prism, base in, is not frequently increased by practice. This, in my experience, makes unreliable the ratio given (prism convergence, or adduction, is to prism divergence, or abduction, as 3 is to 1). Such a ratio is rarely constant, does not help in making a diagnosis and may be confusing testimony.

While the foregoing tests may seem formidable, a little practice will result in a high degree of accuracy in a minimum of time. A great saving of time results in the definite knowledge gained instead of a varying amount of uncertainty on each succeeding visit.

VASCULAR BASIS OF UVEAL DISEASE

ACUTE ANOXIA AS THE FUNDAMENTAL PATHOLOGIC PHYSIOLOGY

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In a recent article [1] I made the statement that "The basic pathology is identical for acute exudative choroiditis, acute spastic closure of the central retinal artery and acute retrobulbar neuritis. This process consists of arteriolar spasm, capillary dilatation and increased capillary permeability with transudation of plasma, white cells and, in severe cases, erythrocytes. . . . This picture will vary, depending on the anatomic structure of the involved tissue, but the differences seen from tissue to tissue and from lesion to lesion are quantitative rather than qualitative. The result is tissue anoxia."

It was pointed out that the factor determining the location of the lesion in the choroid, retina or optic nerve was probably an increased sensitivity of the smooth muscle in the arteriolar wall to some substance in the circulating blood. "The recurrence of similar lesions in the same person would seem to indicate that this vascular sensitivity is of fundamental importance in any study of the causation of acute choroiditis or the other pathologically similar lesions."

Histamine or a histamine-like body was suggested as a likely etiologic agent, because histamine is the only substance occurring normally in the body which can cause arteriolar constriction and capillary dilatation with increased capillary permeability. The degree of increased capillary permeability will determine whether plasma, white cells or erythrocytes pass into the tissues with a resulting perivascular edema, lymphocytic infiltration or an accumulation of red blood cells. These capillary changes can occur if there is an inadequate supply of oxygen to the capillaries, and they can also be produced by large amounts of epinephrine hydrochloride, given intravenously, the capillary changes being ascribed to the anoxia resulting from the intense vasoconstriction.

It was also pointed out that if arteriolar spasm were the fundamental pathologic change in these conditions, vasodilator therapy should be the treatment of choice, because "the purpose of vasodilator therapy is to improve the blood supply to the tissues, thereby relieving the tissue anoxia."

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1. Duggan, W. F.: Acute Exudative Choroiditis: Pathologic Physiology; Treatment with Vasodilators, Arch. Ophth. **23**:930 (May) 1940.

Four of 5 patients with acute exudative choroiditis treated with twelve to fourteen daily intravenous injections of sodium nitrite (0.1 Gm.) attained relatively normal fundi in fourteen, twenty-one, nineteen, and fifteen days, respectively. The final vision was 20/20 for 3 of the patients and 20/30 for the fourth. The fifth patient improved only slightly. One more patient has been treated since then. The vision was 20/200, and there was an acute lesion in the macular region which had been present for three weeks. In one month, following twenty-two injections of sodium nitrite, the vision had improved to 20/20 with ability to read Jaeger's test type 1 and the lesion of the fundus was markedly decreased in size.

Isolated reports of improvement following this therapy in cases of closure of the central retinal artery have been published. Early treatment is usually essential, as in Esterman's case,[2] because the retinal ganglion cells are extremely sensitive to lack of oxygen. While the spasm is often relieved, function frequently fails to return to normal because anoxia has lasted long enough for the ganglion cells to become necrotic. Here the lack of improvement in function can be attributed to the location of the lesion and to the inability of certain cells to withstand relatively short periods of complete anoxia.

Several years ago I reported on the value of vasodilator therapy in cases of acute retrobulbar neuritis.[3] Since then, a total of 29 eyes have been treated by this method. Twenty-five of these eyes attained a final vision of from 20/30 to 20/15 in an average time of nine and seven-tenths days per eye.

In none of the foregoing cases were any other types of therapy used. The visual results were better, and the time required for clinical cure was shorter than with the customary therapeutic procedures.

IRITIS AND CYCLITIS AS A MANIFESTATION OF LOCALIZED TISSUE ANOXIA

For the past two years I have been interested in considering iritis, iridocyclitis and cyclitis as basically similar to acute retrobulbar neuritis, acute exudative choroiditis and acute spastic closure of the central retinal artery or one of its branches. All of these conditions show sharply localized lesions; in all cases there are edema and round cell infiltration which varies only in degree from case to case and from tissue to tissue, and in all these superficially different lesions sharply localized areas of tissue necrosis may occur which are replaced by scar tissue during the healing process.

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2. Esterman, B.: New York State J. Med. **37**:296 (Feb. 1) 1937.

3. Duggan, W. F.: Use of Vasodilators in Treatment of Acute Retrobulbar Neuritis, Arch. Ophth. **16**:380 (Sept.) 1936; Acetylcholine in the Treatment of Acute Retrobulbar Neuritis, ibid. **17**:579 (April) 1937.

The nomenclature of these different conditions is of anatomic origin. The ending, itis, suggests that they are akin to the acute inflammations which result when bacteria invade the tissues, yet they are in no way similar to acute appendicitis or acute mastoiditis. They are obviously not contagious, nor are they comparable to the lesions which occur when pyogenic bacteria gain access to the interior of the eye. They usually occur in relatively normal persons. On very insufficient evidence, focal infection or tuberculosis is assumed to be the cause of most of these lesions.

Recurrences of the various types of uveal disease are probably as frequent as recurrences of acute retrobulbar neuritis or of multiple sclerosis. This indicates a specific tissue hypersensitivity or, more precisely, a localized hypersensitivity of the arterioles and capillaries in a particular tissue to circulating "toxins." However, these "toxins" are often substances occurring normally in the body. As Moon [4] has stated, "many phenomena called toxic are essentially anoxic" and "if all agents which produce relaxation and permeability of capillaries shall be regarded as toxins then the conception of toxemia is substantiated. However, that definition would include normal metabolites, cytoplasmic substances and lack of oxygen as toxins."

Friedenwald [5] mentioned that "in iritis . . . the infiltration is focal, the center of the focus being within the substance of the iris and including at times a small zone of necrosis. There is great edema and distortion of the iris stroma and when the process subsides a defect of the iris is left which is healed by new-formed connective tissue. On the back of the iris under the lesion, a fibrinous exudate develops by which the iris is bound to the lens; and in the organization of this exudate a permanent adhesion between the iris and the lens is produced." Concerning choroiditis, he stated: "On microscopic examination these cases exhibit a dense focal infiltration of the choroid with great swelling and much destruction of tissue. The superficial layers of the choroid, and also the overlying retina, are often necrotic. . . . When healing ultimately takes place, a connective tissue scar replaces the choroid and retina over the affected area." He does not discuss cyclitis as minutely, but an illustration in his book (fig. 37) shows a typical focal accumulation of round cells partially surrounding the circulus arteriosus iridis major.

Obviously all of these lesions can be of vascular origin. They are basically similar but superficially different because of anatomic differ-

4. Moon, V.: Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938.

5. Friedenwald, J. S.: The Pathology of the Eye, New York, The Macmillan Company, 1929.

ences in the tissues concerned. The humble vascular system, especially the terminal units, has been for the most part forgotten as a possible primary cause of these lesions attributed to focal infection. Bacteriology has dominated the investigation, interpretation and treatment of these focal lesions for the last fifty years. If these so-called acute inflammations are analyzed as problems of morbid physiology, it is apparent that most of the conditions ascribed to allergy, focal infection, toxemia and tuberculosis are fundamentally manifestations of acute localized tissue anoxia. In many cases overaction or underaction of homeostatic mechanisms as modified by climate, dietary insufficiency and the endocrine glands shifts the reactions in the tissues from the zone of normal physiology into the zone of pathologic physiology, which consists of arteriolar spasm, increased capillary dilatation and permeability and round cell infiltration. At this stage vasodilator therapy can bring about a complete and rapid restitution to normal. If pathologic physiology progresses to the stage of pathologic anatomy, as evidenced by focal necrosis and scar tissue formation, vasodilator therapy can ameliorate the condition and prevent any further destruction of tissue, but it cannot effect a complete return to normal anatomic structure and normal function.

In iritis the focal lesion is usually in the posterior half of the stroma, where the blood vessels are found. Because of the crypts on the anterior surface of the iris, the edema fluid, which contains plasma proteins and lymphocytes, passes into the anterior chamber, giving rise to the aqueous flare and the cells in the aqueous. The fact that the lesions are often near the lesser arterial circle of the iris accounts for the synechiae, the seclusion or occlusion of the pupil and the secondary glaucoma which often develops. When the lesion is in the ciliary body the greater mass of tissue can give rise to more white cells and protein, accounting for the vitreous haze and the posterior corneal deposits. Likewise, the coating of the ciliary body with transudate and its organization by connective tissue explain the secondary phthisis.

Therefore, the same basic lesion can produce glaucoma if it is located in the iris and phthisis if it is located in the ciliary body. It must be stressed that the glaucoma and phthisis are secondary and that their development depends on the anatomic structure of the anterior segment of the eye. A similar lesion in the choroid rarely produces marked changes in tension. When these angiospastic lesions are situated in the retina or the optic nerve, the ocular tension is not appreciably altered.

TUBERCULOSIS AND SYPHILIS

In uveal lesions attributed to tuberculosis and syphilis, the pathologic process is perivascular and differs only in degree from the simple cases. Even the giant cells and epithelioid cells may develop only in con-

sequence of a prolonged period of anoxia, since tubercle bacilli are rarely found and spirochetes, when present, are relatively few in number. In addition, tubercle bacilli and spirochetes, when present, may have lodged in a locus minoris resistentiae, just as in carbon monoxide poisoning dyes accumulate in perivascular regions. Findlay [6] has shown that after subcutaneous injections of histamine in animals subsequent intravenous injection of bacilli resulted in their lodging almost exclusively in the regions injected with histamine. And Kennedy, Wortis and Wortis [7] stated: "It is common knowledge that vascular accidents occur in the brain in the course of untreated luetic infection. The very fact that many of these episodes are rapid to occur and clear up without treatment is evidence in favor of the possibility of angiospasm being the causative mechanism. Surely, luetic invasion of cerebral blood vessels must at times be an irritation adequate to set up local reflex angiospasm in these vessels."

It is still a question in my mind whether the vascular changes in the eye or brain occur first and the spirochetes lodge secondarily or vice versa. And what of the cases in which the changes occur while patients are under treatment? It is possible that the acute vascular catastrophes occurring in the brain, optic nerve or iris are a direct toxic effect of arsenic on hypersensitive arterioles and/or capillaries.

SYMPATHETIC OPHTHALMIA

The typical focal lesion described here may involve one small sector of the iris; the whole iris; the iris and ciliary body; the iris, ciliary body and choroid and, finally, the iris, ciliary body, choroid and optic nerve, causing the condition known clinically as Harada's disease. From Harada's disease to sympathetic ophthalmia is only a short step, since the former is not preceded by a perforating injury and the latter usually is. Both are identical in all other respects. Some observers have stated that sympathetic ophthalmia is limited to the uveal tract. This is not true. I recall one case in which there were deafness and falling out of the eyebrows and another case in which there were temporary mental derangement, loss of the hair on the head and an increased growth of hair on the face. Sympathetic ophthalmia is a prolonged, severe, exaggerated lesion which differs only in degree from the milder and commoner varieties of uveal disease.

Some ophthalmologists believe that sympathetic ophthalmia is due to infection by a relatively harmless germ which has a special predilection

6. Findlay, cited by Topley.[8]

7. Kennedy, F.; Wortis, S. B., and Wortis, H.: Clinical Evidence for Cerebral Vasomotor Changes, New York State J. Med. **38**:1441 (Nov. 15) 1938.

for uveal tissue. This theory is not supported by the known facts. Others believe that it is due to allergy, especially allergy to uveal pigment. This seems unreasonable. However, the concept of allergy can be accepted if by allergy one means only a lesion characterized by hypersensitivity of arteriolar muscle and an increased capillary permeability. If previous sensitization is a necessary prelude to allergy, then the term "hypersensitivity" is preferable, since this would also include cases in which the disease is due to an abnormal response to histamine or histamine-like bodies. Moreover, previous sensitization to histamine is not necessary in order to evoke reactions, and injections of histamine mimic anaphylaxis in animals and allergy in man.

According to Topley,[8] the most dramatic features of anaphylactic shock are the result not of the antigen-antibody reaction itself but of the liberation of histamine by the injured cells and the secondary response of the histamine-sensitive cells throughout the body.

Traumatized tissue liberates histamine; cold liberates it in the skin; focal infections may liberate it, and it is formed in the intestine by bacterial decomposition of proteins. Moreover, its removal is oxidative, either directly or through the mediation of histaminase.[9]

Code[10] has reported that a histamine-like substance could be extracted from blood and that most of this substance was found in the leukocytes. Since these focal lesions are accompanied by a perivascular infiltration of round cells, which is extreme in sympathetic ophthalmia, and since these focal lesions are anoxic in origin and may become necrotic, it must be apparent that histamine or a histamine-like substance could be liberated from these lesions. It could then diffuse slowly to adjacent regions in the same eye or via the blood stream to histamine-sensitive cells elsewhere in the body, which in the case of sympathetic ophthalmia are in the opposite eye. If this is true, and I think it is, one has a situation in which introduction of a small amount of a specific nonliving substance into the tissues sets up a self-perpetuating mechanism whereby more and more of the substance causing the initial lesion is formed, so that a vicious circle results: Histamine causes a focal area of tissue anoxia; because of the anoxia, a focal necrosis results, with liberation of more histamine; this histamine acts on nearby or distant histamine-sensitive cells, leading to the development of more anoxic regions, which, as new sources of histamine, can both intensify the reac-

8. Topley, W. C.: An Outline of Immunity, Baltimore, William Wood & Company, 1933.

9. Best, C. H., and McHenry, E. W.: Histamine, Physiol. Rev. **11**:371 (Oct.) 1931.

10. Code, C. F.: Source in Blood of Histamine-Like Constituent, J. Physiol. **90**:349 (Aug. 17) 1937.

tion in the original focus and also lead to the development of more lesions. Obviously, one has a self-perpetuating mechanism set in motion which is not due to a living organism but is primarily biochemical in nature. This hypothesis adequately explains both the usual cases of sympathetic ophthalmia and atypical cases, such as those secondary to choroidal sarcoma.

The objection could be raised that the small amounts of histamine produced in these focal lesions would be insufficient to cause the development of more lesions. Maijala [11] reported the case of a 32 year old man with syphilitic aortitis who died a half-hour after receiving 0.8 mg. of histamine subcutaneously! If 0.8 mg. could produce death in a person hypersensitive to histamine, surely infinitesimal amounts could produce these relatively small ocular lesions in hypersensitive persons.

The positive Mantoux reaction, on which the diagnosis of tuberculosis is based in acute iridocyclitis and acute choroiditis, is of little or no diagnostic value in adults. Corelli [12] reported that the subcutaneous injection of 0.8 or 1 mg. of histamine caused intensification of positive reactions to cutaneous and intradermal injections of tuberculin. Therefore, a positive tuberculin reaction or a positive reaction to other cutaneous tests does not necessarily indicate specific infections. Such positive reactions may only mean that there is histamine in the circulating blood. Therefore, in adults these positive cutaneous reactions may actually be indicative of histamine hypersensitivity.

TREATMENT

In the past the treatment of uveal disease has included the use of mydriatics, salicylates, hot compresses, epinephrine packs, sulfanilamide, diathermy, artificial fever therapy, short wave therapy and iontophoresis, the injections of gold compounds, foreign protein and vaccines, the production of sweats, the removal of questionable foci of infection and the administration of gallons of tuberculin. The fact that the condition sometimes becomes worse or develops in the other eye after the use of some of the more drastic types of therapy permits a reasonable doubt as to their actual value.

Mydriatics of the atropine group are of value chiefly because of their action in dilating the pupil and preventing the formation of synechiae. They also are said to have a mild vasodilating action which may affect disease of the uveal tract favorably. However, this action must be relatively unimportant because cases of sympathetic ophthalmia have

11. Maijala, P.: Death Due to Histamine: Case, Nord. med. tidskr. **16**: 1287 (Aug. 13) 1938.

12. Corelli, F.: Intensification of Cutaneous and Visceral Allergy from Histamine Injections, Policlinico (sez. med.) **44**:491 (Oct.) 1937.

developed in which the primarily affected eye has been thoroughly atropinized prior to the onset of the sympathetic disease.

Epinephrine hydrochloride, which is used to dilate the pupil in iritis and iridocyclitis, may, by increasing the arteriolar constriction, lead to an increase in the tissue anoxia and aggravate the condition. This could explain why the pain is sometimes increased in these eyes after the use of this drug. I think it should be used only once in order to break any synechiae which may be present. Its continued use is probably harmful.

For the reasons just outlined at length, namely, that disease of the uveal tract and acute retrobulbar neuritis are fundamentally the same disease, both being a manifestation of acute localized anoxia of arteriolar-capillary origin, and that different types of lesions in the same tissue differ quantitatively rather than qualitatively, I wish to report the results of vasodilator therapy in 11 cases of iritis, iridocyclitis and cyclitis. In the beginning the treatment was used only in cases in which routine therapy had failed to bring about improvement. In the later cases vasodilators were used immediately with only sufficient atropine to keep the pupil dilated.

REPORT OF CASES

CASE 1.—*Acute Iritis, Recurrent.*—M. Z., a man of 28, had acute iritis of the left eye in July 1935, while being treated for gonorrheal urethritis. Treatment was started on the fourth day, and thirty-five days of treatment were required for cure. On March 4, 1937, he had an attack in the right eye, which became worse after injections of gonococcus vaccine. Seventy-three days of treatment were necessary for cure this time.

On Feb. 11, 1938, he was seen with a fresh attack in the right eye. There was a synechia nasally, with marked circumcorneal injection and tearing. Treatment consisted of the instillation of atropine, the application of hot compresses and the administration of salicylates. On March 2 the condition was worse, and the eye was very soft. The patient was then ordered to use 30 mg. of erythrityl tetranitrate twice daily by mouth for one week. He felt better on March 3. On March 4 the eye was definitely whiter, and there was no tenderness or pain. On March 9 the vision was 20/30, and the eye was practically white. On March 18 there was a recurrence of circumcorneal injection; so he was given 0.1 Gm. of sodium nitrite intravenously; one hour later the eye was whiter. The injection was repeated on March 20. The patient was last seen on March 23 when the eye was still quiet.

The patient used atropine throughout the treatment. Routine treatment for nineteen days was not followed by any improvement. The addition of erythrityl tetranitrate to his therapy was followed by a marked and sudden improvement. He was cured clinically in seven days.[13]

13. The time required for clinical cure is calculated from the date on which vasodilator therapy was instituted for all cases described.

A slight flareup nine days later disappeared after one injection of sodium nitrite.

CASE 2.—*Acute Iritis.*—F. T., a man of 60, had acute iritis of the right eye which was clinically cured in eleven days with routine therapy. There were permanent synechiae. The Wassermann reaction of the blood was negative. Forty years earlier the patient had had gonorrhea.

On June 3, 1938, he was seen with a fresh attack of iritis in the left eye; scopolamine and salicylates were ordered. On June 9 the condition was much worse; the pupil was small, and there were marked circumcorneal injection and pain and a fibrinous exudate in the anterior chamber. Atropine was then used daily, and he received 0.1 Gm. of sodium nitrite intravenously on June 10, 11, 12, 17 and 18. There was progressive improvement. On June 17 the eye was definitely improved, and the exudate had broken up and partially absorbed. On June 22 the anterior chamber was clear. On June 24 the eye was white, the vision was 20/30— and there were permanent synechiae. When the patient was seen last, on Feb. 17, 1939, the vision was 20/20 and there had been no recurrences.

In spite of the use of mydriatics, hot compresses and salicylates, this patient became steadily worse for six days. As soon as vasodilator therapy was started, there was immediate improvement, so that he was clinically cured in fourteen days.

CASE 3.—*Acute Iridocyclitis Following Removal of Tooth.*—H. H., a man of 28, was seen on April 29, 1938, with acute iridocyclitis of the right eye of seven days' duration. It began one to two days after extraction of the upper right first molar tooth.

The vision was 20/70; this corrected to 20/30— with concave lenses. In addition to marked circumcorneal congestion, the iris was swollen, dilated venules were visible on its anterior surface, the anterior chamber was full of cells and the disk was seen indistinctly. There was a synechia nasally. The patient was given 1 drop of scopolamine daily and five daily intravenous injections of sodium nitrite.

There was slow but steady improvement. On May 6 the eye was white, the pupil was dilated, the aqueous was clear and the iris appeared normal. When the patient was seen last, on May 27, the vision was 20/20— (without correction), and there were no evidences of the iritis except for a few old deposits on the back of the cornea and pigment on the lens at the site of the synechia present at the first visit. This patient, on his own authority, had another tooth removed on May 5, when the eye was essentially over the attack.

The patient received a mydriatic once daily and five injections of sodium nitrite. Clinical cure resulted in seven days.

CASE 4.—*Acute Iritis, Recurrent.*—J. P., a man of 52, was seen on June 12, 1938, with the complaint of pain, tearing, redness and photophobia in the left eye for two days. The vision in this eye was 20/20, and there were moderate circumcorneal congestion and an aqueous flare. The pupil was adherent to the iris everywhere except at two small points. He had suffered from arthritis for seven years and gave the history of a mild attack of iritis in the left eye several years previously. The Wassermann reaction of the blood was negative, and the patient stated that he had never had gonorrhea.

He received five daily intravenous injections of sodium nitrite (0.1 Gm.), and 1 drop of atropine was instilled daily for five days. He then took 15 mg. of erythrityl tetranitrate twice daily for two weeks. There was immediate improvement. On the fifth day the eye was white, there was no pain or tenderness, the pupil was fully dilated and the aqueous showed only an occasional cell. He was seen regularly until August 1939. The vision remained normal, and there were no recurrences up to that time.

The patient received intensive vasodilator therapy, an epinephrine pack on the first day and 5 drops of atropine. The time of clinical cure was five days.

CASE 5.—*Acute Iritis; Syphilis.*—C. S., a Negro of 41, was seen on Aug. 10, 1938 because of the sensation of a foreign body in the right eye. No foreign body was found. He returned on August 13, at which time the vision was 20/200, there was marked circumcorneal injection, the iris was swollen, there was an early synechia, the aqueous was full of cells and the fundus could not be seen clearly.

The pupil was dilated with cocaine and epinephrine hydrochloride. The patient received atropine once daily for a week and eight intravenous injections of sodium nitrite between August 13 and 21. Beginning on August 18 he took 30 mg. of erythrityl tetranitrate by mouth twice daily for one week.

There was marked and rapid improvement. On August 15 the vision was 20/50, the eye was almost entirely white, there was no pain or tenderness and the cells in the aqueous had decreased. On August 18 the eye was entirely white. The Wassermann reaction of the blood was 4 plus; so he started antisyphilitic treatment on August 21.

The patient received no treatment except vasodilators and atropine once daily for seven days. The time of clinical cure was five days. In spite of a positive Wassermann reaction, antisyphilitic treatment was not started until the iritis was cured.

CASE 6.—*Chronic Iridocyclitis.*—F. M., a woman of 25, was seen on Oct. 3, 1938 because of blurred vision in the right eye and redness of both eyes for three weeks. She had had recurrent attacks of iridocyclitis in both eyes for several years. She had been using atropine and hot compresses for one week.

The vision of the right eye was 20/30—. There were slight circumcorneal congestion and many posterior corneal deposits, the iris markings were blurred and the vitreous was hazy.

The vision of the left eye was reduced to perception of hand movements. This eye showed, in addition to the changes noted in the right eye, a complicated cataract, a postoperative coloboma of the iris and many posterior synechiae.

The patient continued to use atropine and hot compresses and was given six daily intravenous injections of sodium nitrite (0.1 Gm.) followed by 15 mg. of erythrityl tetranitrate by mouth twice daily for two weeks.

On October 7 there was definite improvement. The eyes were whiter, both irides were flat and the vision in the right eye was 20/30. On October 14 the eyes were completely white, and the vitreous was clear. On November 2 the vision was 20/20—. The patient was seen last on March 1, 1939, at which time there had been no further recurrences.

The patient had had repeated low grade attacks of iridocyclitis and had lost useful vision in her left eye. A fresh attack was not materially ameliorated until vasodilator therapy was employed. The time of clinical cure was eleven days.

CASE 7.—*Acute Iritis, Recurrent.*—S. G., a man of 52, had an attack of acute iritis in the right eye on Jan. 1, 1939. All extraocular examinations gave negative results, and the history revealed nothing of significance except for gonorrhea at the age of 19. In spite of intensive treatment with atropine, hot compresses and salicylates, the condition of the eye steadily became worse until on January 12, when the vision had decreased to 10/200 because of exudate in the anterior chamber; the patient was admitted to the hospital for intravenous injections of typhoid vaccine. There was slow improvement until January 22, when he was discharged with normal vision and a white eye.

On March 9 he was seen with a fresh attack in the same eye, of one day's duration. He had used atropine before I saw him. Between March 9 and 16 he received six intravenous injections of sodium nitrite (0.1 Gm.) and used atropine once daily. He continued the use of hot compresses because they had been ordered for his first attack. There was daily improvement. On March 18 the eye was practically white, and on March 21 it was completely normal. No further recurrences developed during 1939.

The patient's first attack of iridocyclitis lasted twenty-one days and required hospitalization and foreign protein therapy. The iridocyclitis of the second attack began to clear up as soon as vasodilator therapy was instituted. The time required for clinical cure was ten days.

CASE 8.—*Acute Iritis, Recurrent.*—J. B., a man of 36, was seen on Feb. 6, 1939, with the history that the right eye had been red, painful and tearing for one week. One year before he had a similar attack in the same eye coincidental with a gonorrheal urethritis, which was treated at that time.

The vision in the right eye was 20/70. There was marked circumcorneal injection, the aqueous was turbid, there was a small amount of fluffy exudate in the lower part of the pupil and the iris was edematous, with dilated venules visible on its anterior surface. With an epinephrine pack the pupil dilated except down and out, where there was an old adhesion. An ointment containing atropine was placed in the eye.

The patient was seen next on February 8. The vision was 8/200, the pupil was constricted, the lower half of the anterior chamber was completely filled with exudate and there was some exudate adherent to the back of the cornea. No red reflex could be elicited in the pupillary area. There were marked pain and tenderness. The patient refused to enter the hospital, so, beginning on February 8, he received six daily intravenous injections of sodium nitrite, followed by three more on February 17, 18 and 19. Also, starting on February 13 he took 30 mg. of erythrityl tetranitrate twice daily by mouth.

On February 10 the vision was 20/30; all of the exudate in the anterior chamber had disappeared, except some that still remained adherent to the back of the cornea; the iris was flatter and less congested, and there was a normal red fundus reflex. On February 13 the aqueous was clear, and the circumcorneal injection had disappeared above the cornea and was markedly decreased below. There was no pain or tenderness at this time. The eye slowly whitened. On

February 23 it was white, and the vision was 20/20—. With the slit lamp a few precipitates could be seen on the back of the cornea. The patient received atropine in sufficient amount to keep the pupil dilated, usually a drop every second or third day.

The iritis in this case was of the type ascribed to gonorrhea. With minimal amounts of atropine and intensive vasodilator therapy, the recovery was as rapid and the relief of signs and symptoms was as good or better than in cases in which the customary methods of treatment were used. The time required for clinical cure was fifteen days.

Case 9.—*Postoperative Iridocyclitis.*—C. Y., a woman of 58, had a combined extracapsular extraction for a nuclear cataract in the right eye on Aug. 2, 1939. No complications occurred during the operation. The patient had had trachoma during her youth, and there were many old corneal opacities.

After the operation there was a moderate amount of cortex. The eye became injected, and there was marked tearing. The patient received several injections of milk and large amounts of atropine and salicylates. When she was discharged on August 23 the eye was soft, injected and tearing, and there was a rather dense membrane which filled the pupillary area. She was told to use atropine, hot compresses and 10 grains (0.65 Gm.) of sodium salicylate three times daily at home.

On August 28 a few posterior corneal deposits were seen. On September 1 the condition was worse: The eye was softer, the corneal deposits were increased, the tearing and redness were more marked and there was moderate pain.

The administration of salicylates was discontinued, the amount of atropine was reduced to 1 drop twice a day, 15 mg. of erythrityl tetranitrate was given twice daily by mouth and an intravenous injection of sodium nitrite (0.1 Gm.) was given on September 1, 2, 6 and 8.

On September 6 there was no pain or tearing, the tension had improved, the cortex was absorbing and the redness of the eye had disappeared except in the region of the operative wound. On September 11 the eye was entirely white, and the tension was normal by palpation. The patient was seen last on September 22. At this time the eye appeared normal; an opening had appeared in the secondary membrane through which a good red reflex was obtained, and the vision was 5/200. Dr. E. Lyon later performed a discission on this eye. There had been no recurrence of the iridocyclitis when she was last seen by him, in May 1940.

This case is of interest because a low grade iridocyclitis developed after cataract extraction which did not respond to any treatment in the hospital. With the decrease in tension and increase in corneal deposits, the condition could have been called endophthalmitis phacoanaphylactica or sympathetic ophthalmia in the early stage. The eye would probably have become phthisic. With the institution of vasodilator therapy there was an immediate arrest in the iridocyclitis, and the eye was clinically cured in ten days.

Case 10.—*Acute Iridocyclitis, Recurrent; Syphilis.*—C. A., a Negro of 34, was seen on Aug. 21, 1939, with the complaint of severe pain, tearing, redness and photophobia of the left eye for one week. He gave the history of two

previous attacks in the same eye and of gonorrheal urethritis in 1932. At the time of the present attack he had been receiving antisyphilitic treatment for one year at the Board of Health of New York City.

The vision in the left eye was 10/200 and could not be improved. There were marked circumcorneal injection, marked tenderness of the globe and a large mass of jelly-like exudate filling about one fifth of the anterior chamber. The iris was muddy and edematous, there were many synechiae and the vitreous was so hazy that no details of the fundus could be seen. The right eye was normal.

After the use of an epinephrine pack, the pupil dilated irregularly to about a diameter of 5 mm. (Adhesions from previous attacks prevented full dilatation.)

The patient received 0.1 Gm. of sodium nitrite intravenously August 21 to 25 inclusive, August 30 to September 1 inclusive and on September 6, a total of nine injections. The only other medication used was 1 drop of atropine on August 21, 23 and 30.

On August 23, two days after treatment was started, the vision was 20/70, there was no pain or tenderness, the eye showed only a faint trace of circumcorneal injection, the exudate in the anterior chamber had been reduced to a particle no larger than the head of a pin and the vitreous was clearer. On August 30 the eye was entirely white, the uncorrected vision was 20/40, there were only a few cells in the anterior chamber and the eye was clinically cured. On September 18 the corrected vision was 20/20—, and the eye was still quiet.

The patient showed the most rapid improvement of any patient in the series, as he was practically over the attack after four days (on August 25). It was necessary to send a social worker to his home to get him back for examination on August 30. While the iridocyclitis occurred at the time the patient was receiving antisyphilitic treatment, it resembled, clinically, the type attributed to gonorrhea. It could have been a toxic reaction following arsenical therapy. In spite of the severity of the iridocyclitis, the patient was not hospitalized, nor were hot compresses, salicylates or injections of foreign proteins prescribed. In addition to the vasodilator therapy, only 3 drops of atropine were used. The time required for clinical cure was nine days. Since the patient was almost well after four days, the actual time of cure was probably less than nine days.

CASE 11.—*Cyclitis.*—G. C., a man of 28, was seen on Aug. 28, 1939, with the complaint that the right eye had been red and tearing for four weeks. The vision was 20/30, there was a broad zone of purplish circumcorneal injection, the iris markings were a little indistinct, there were a few cells in the aqueous and a few tiny deposits were visible on the back of the cornea. The pupil dilated fully with 1 drop of scopolamine. The evidences of iritic involvement were so slight that in the absence of photophobia and synechiae the condition was diagnosed as cyclitis. While there was no history of a preceding illness, the lesion resembled the cyclitis seen after influenza.

On September 1, after five daily intravenous injections of sodium nitrite (0.1 Gm.) the tearing had stopped and the eye was much whiter. The patient then took 30 mg. of erythrityl tetranitrate twice daily by mouth. On September 6 the vision was 20/20; there were no symptoms, but there was still a trace of congestion. He received six more injections of the sodium nitrite between September 6 and 18. On the latter date there was still a trace of congestion below the

cornea. The patient received no other treatment except 1 drop of scopolamine on August 28 and another on September 8.

This case was one of cyclitis of four weeks' duration characterized by marked circumcorneal injections, minimal symptoms and only a few posterior corneal deposits. Patients with similar involvement are often hospitalized for several weeks and subjected to the production of sweats, foreign protein therapy, intensive atropinization, and other unpleasant treatments. With only vasodilator therapy and 2 drops of scopolamine, improvement was as rapid or more rapid than is usual in cases in which drastic methods are used. The slow whitening of the eye was probably due to the fact that the condition had been present for four weeks and the episcleral vessels had lost their "tone." While it required nine days for the eye to become practically white, the patient was free from symptoms after about five days.

SUMMARY

Eleven cases of acute uveal disease exclusive of choroiditis have been described in which vasodilator therapy seemed to be of definite value. Because the series is short, a statistical analysis of the results is not possible.

As the cases varied both in type and in degree, it can only be said that recovery was slightly more rapid in patients seen early and in those seen during a first attack. In several instances the customary therapeutic procedures had not been followed by any improvement; as soon as vasodilator therapy was instituted, improvement occurred.

The time required for clinical cure varied between five and fifteen days; the average time was nine days.

No patient was hospitalized. Five patients (cases 2, 5, 8, 9 and 10) would ordinarily have been hospitalized; they were cured in an average time of ten and six-tenths days. Two patients (cases 3 and 7) might have been hospitalized; the average time of cure for them was eight and a half days. The other 4 patients would not ordinarily have been hospitalized; the average time of cure for them was seven days.

Mydriatics do not prevent attacks, as was evident in the case in which one occurred after operation, nor can they be depended on to effect a cure, as was shown by the patients who became worse while receiving atropine several times a day. Their main function is to dilate the pupil, though they may, according to some authorities, have a mild vasodilating action. As more patients were treated, the use of mydriatics was decreased, so that the tenth patient received only 3 drops of atropine and the eleventh received only 2 drops of scopolamine.

After vasodilator therapy is instituted there is usually a lapse of two or three days before marked clinical improvement is obvious. Signs and symptoms in these cases disappeared in the following order: pain,

tearing, photophobia and tenderness; exudates in the anterior chamber; edema of the iris and cells in the aqueous; vitreous haze, and, finally, circumcorneal injection. Visual improvement occurred coincidentally with the absorption of exudates and clearing of the vitreous.

Six patients were seen during a recurrent attack in the same eye. Three of these had had gonorrhea, and 1 had had both gonorrhea and syphilis. Three patients gave the history of an attack in the opposite eye prior to the time I saw them.

Five patients gave a history of gonorrhea, but in 2 cases there was an interval of more than thirty years between the urethritis and the iritis or iridocyclitis.

Two patients had syphilis. This was not of unfavorable prognostic significance. The patient who had not received antisyphilitic treatment was cured clinically in five days, while the patient who had been receiving antisyphilitic treatment for a year was completely cured in nine days. As the latter was delinquent in returning to the clinic, the actual time of cure was probably less than nine days. Both of these patients had severe involvement and would ordinarily have been hospitalized.

The condition in 1 case occurred after an uncomplicated cataract extraction. It could have been diagnosed as either endophthalmitis phacoanaphylactica or as sympathetic ophthalmia in the early stage. The response to vasodilator therapy was excellent.

The lesion in 1 case occurred within forty-eight hours after the extraction of a tooth. Since teeth are often removed to "cure" an iridocyclitis, this permits a reasonable doubt as to the value of such a procedure.

CONCLUSIONS

The marked and rapid improvement which occurs in cases of iritis, iridocyclitis and cyclitis when intensive vasodilator therapy is employed is of fundamental biologic importance. The similarity between these three conditions and acute choroiditis, acute spastic closure of the central retinal artery or one of its branches and acute retrobulbar neuritis is based on the fundamental pathology and pathologic physiology of the lesions. The early changes consist of arteriolar constriction, capillary dilatation and increased capillary permeability with resulting perivascular edema and round cell infiltration. The superficial differences between these clinical lesions depend on the anatomic structure of the tissues involved in these focal lesions. The early pathologic changes are due to capillary anoxia, which in turn causes localized areas of tissue anoxia. The late pathologic changes are usually due to the replacement of acute focal necroses by scar tissue.

Histamine or a histamine-like body is suggested as a likely etiologic agent because (1) histamine constricts arterioles and both dilates and

increases the permeability of capillaries; (2) histamine can account for cases ascribed to allergy, focal infection and cold, and (3) histamine is set free when tissue is traumatized.

Hypersensitivity of one or more arteriolar-capillary units to histamine or a histamine-like body explains the focal nature of these lesions. Arteriolar and capillary hypersensitivity may be due to an excess or deficiency of epinephrine and the other hormones, to a relative avitaminosis and probably to an age factor. A relative lack of histaminase may be the factor whereby histamine or a histamine-like body is able to enter the circulation in one region of the body and act on histamine-sensitive cells at some remote point in the body.

Sympathetic ophthalmia differs only quantitatively from the ordinary case of iridocyclitis. The giant cells and epithelioid cells are merely the reaction of uveal tissue cells to prolonged anoxia. A new theory is offered for the origin and development of sympathetic ophthalmia which is based on the pathologic and clinical features of this condition. Moreover, it satisfactorily accounts for the atypical cases not preceded by a perforating injury. A similar mechanism would explain cases of sarcoid, Hodgkin's disease and many diseases attributed to viruses.

While the causation is often obscure in uveal disease, the arteriolar and capillary changes are the final common pathway for all lesions attributed to focal infection, to allergy and to a lack of the different vitamin B factors (particularly thiamine and nicotinic acid). Treatment directed specifically toward the vascular pathologic process has produced excellent therapeutic results.

Vasodilators which act favorably in all cases showing pathologic involvement which can be attributed to histamine or a histamine-like body seem to be almost a specific for these acute vascular catastrophes. The function of vasodilators is to insure an adequate supply of oxygen-containing blood to the tissues, thereby relieving the tissue anoxia.

I hold no brief for intravenous sodium nitrite per se. Its use will not prevent later attacks. It may not be needed in most cases of mild iritis and iridocyclitis. There probably are cases in which it will not be of any help. However, in cases of severe involvement and probably in cases of sympathetic ophthalmia, its use is more logical and should be fully as effective as is the use of salicylates, sodium cinchophen, foreign protein therapy, fever therapy, sulfanilamide, the injection of vaccines and the production of sweats. Moreover, it produces no general discomfort or pain. In time, some preparation may be found which can be given by mouth. At the present time erythrityl tetranitrate seems best suited for oral administration. Histaminase may be found to be of value as an adjunct in the treatment of these acute vascular catastrophes.

E. Tosse & Co. supplied ampules of 10 per cent sodium nitrite for trial in many of these cases.

MYOPIA AFTER USE OF SULFANILAMIDE

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Toxic manifestations of sulfanilamide have occupied the attention of the clinicians and experimenters since Domagk's initial paper on the drug in 1935.[1] A multiplicity of disorders have been discovered, and new ones are constantly being reported; these range from the common complaint of nausea and dizziness [2] to the fatal reactions such as granulopenia.[3] Cases of acidosis,[4] cyanosis,[5] various anemias,[6] methemoglobinemia,[7] sulfhemoglobinemia,[8] dermatoses,[9] fever [10] and nephritis [11] have all been demonstrated.

Read at the clinical staff meeting of the McKeesport Hospital, March 26, 1940.

Dr. John Alexander of Pittsburgh extended the use of the Department of Literary Research, American College of Surgeons, and Dr. Andrew Hunter of McKeesport gave me his aid.

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(Footnotes continued on next page)

Bucy [12] reported the first ocular reaction to the drug. A 16 year old girl who ingested a small amount of the medicine displayed a marked idiosyncrasy; cyanosis and headache developed, followed by optic neuritis with central scotoma.

A review of the literature shows that 2 cases of myopia reportedly due to the administration of sulfanilamide have taken place in this country and that 3 or possibly 4 cases of a similar reaction have been reported from Europe, 1 of this number being due to sulfapyridine.

Landsberg [13] reported a case in which a white man aged 33 who received sulfanilamide for a gonorrheal infection showed definite myopia, which cleared up five days after the administration of the drug was stopped. The myopia was correctable by lenses. No ciliary spasm or optic neuritis was discovered.

Spellberg [14] also reported a case in which a white man aged 41 took 30 grains (1.94 Gm.) of sulfanilamide for gonorrhea without a reac-

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8. Archer, H. E.: Sulfhemoglobinemia: Its Cause and Prevention, Lancet **2**:432, 1937. Daniela, A. P.: Sulfhemoglobinemia Due to Simultaneous Use of Magnesium Sulfate and Sulfanilamide, Nederl. tijdschr. v. geneesk. **81**:1837, 1937. Patou, J. P. J., and Eaton, J. C.: Sulfhemoglobinemia and Methemoglobinemia Following Administration of Sulfanilamide, Lancet **1**:1159, 1937. Kane, F. F.: Sulfhemoglobinemia Following Administration of Drugs of Sulfonamide Group, Ulster M. J. **6**:144, 1937. Frost, L. D. B.: Sulfhemoglobinemia Following Antistreptococcal Chemotherapy with Benzyl-Sulfanilamide and Derivatives, Lancet **1**:510, 1937. Discombe, G.: Sulfhemoglobinemia Following Sulfanilamide Treatment, ibid. **1**:626, 1937. Bensley and Ross.[7b]

9. Goodman, M. H., and Levy, C. S.: Development of Cutaneous Eruptions During Administration of Sulfanilamide, J. A. M. A. **109**:1009 (Sept. 25) 1937. Myers, G. B.; Vonder Heide, E. C., and Balcerski, M.: Exfoliative Dermatitis Following Sulfanilamide, ibid. **109**:1983 (Dec. 11) 1937. Schonberg, I. L.: Purpuric and Scarlatiniform Eruption Following Sulfanilamide, ibid. **109**:1035 (Sept. 25) 1937. Finney, J. O.: Severe Dermatitis Medicamentosa Following Administration of Sulfanilamide, ibid. **109**:1982 (Dec. 11) 1937. Menville, J. G., and Archinard, J. J.: Skin Eruptions in Patients Receiving Sulfanilamide, ibid. **109**:1008 (Sept. 25) 1937. Newman, B. A., and Sharlit, H.: Sulfanilamide: Photosensitizing Agent of Skin, ibid. **109**:1036 (Sept. 25) 1937. Brunsting, L. A.: Sulfanilamide Dermatitis: Question of Relation to Photosensitivity, Proc. Staff Meet., Mayo Clin. **12**:614, 1937. Schwentker, F. F., and Gelman, S.: Sulfanilamide Rash, Bull. Johns Hopkins Hosp. **61**:136, 1937. Frank.[4a] Unshelm.[4b]

10. Hageman, P. O., and Blake, F. G.: Specific Febrile Reaction to Sulfanilamide: Drug Fever, J. A. M. A. **109**:642 (Aug. 28) 1937. Bliss and Long.[2]

11. Hanns, A., and Mangeney, L.: Nephritis Due to Use of Prontosil, Strasbourg med. **97**:148, 1937.

12. Bucy, P. C.: Toxic Optic Neuritis Resulting from Sulfanilamide, J. A. M. A. **109**:1007 (Sept. 25) 1937.

13. Visual Disturbance and Sulfanilamide, Queries and Minor Notes, J. A. M. A. **113**:2260 (Dec. 16) 1939.

14. Spellberg, M. A.: Toxicity of Sulfanilamide: Severe Transient Myopia Following Use of Sulfanilamide, Illinois M. J. **75**:366, 1939.

tion; however, eight weeks later, after taking 2 doses (1⅑ grains [0.11 Gm.]) of the drug, he had a severe reaction. Vision decreased to 20/200 in the right eye and 15/200 in the left eye, but a —2.50 and a —2.75 sphere respectively gave normal vision. Dr. A. H. Herman, who examined the eyes, reported normal disks and blood vessels but an apparent edema of both retinas. The picture of the blood was normal. Vision was normal within two weeks after the administration of the drug was stopped.

Lagrange and Laudat [15] reported a case in which a white woman aged 32 took 1.50 Gm. of sulfanilamide daily for ten days without any ill effects. Fourteen days after suspension of the medication, she again took a dose of the same medicine. Six and a half hours later she noticed visual disturbances, her face was bloated and excessively flushed and the conjunctiva was a violet red.

Ophthalmologic examination showed bilateral myopia corrected by a —4.50 sphere. The pupils reacted well. The fundi showed nothing unusual. In a week the eyes were normal.

Another case was reported by Heinonen.[16] A white woman aged 42 took a 0.3 Gm. tablet of sulfanilamide in the evening for a throat ailment. The following day examination revealed myopia amounting to —1.25 D. In the course of four days the eyes were emmetropic. The blood sugar was normal. Heinonen also mentioned another case in which a woman aged 67 complained of severe temporary visual disturbance after taking 56 tablets of sulfanilamide. Unfortunately, no ocular examination was done.

The only case of visual disturbance following the use of sulfapyridine was noted by Fänge.[17] His patient was a white woman aged 21 who had pneumonia. She was treated by a total of 85 Gm. of sulfapyridine during thirty days. She was apparently well when the disturbance of vision took place, requiring a —6.00 and a —7.00 lens for correction. The condition was no different after atropine was instilled. The fundi were normal. Vision was normal in a week. The picture of the blood, including the blood sugar, was normal.

A report of my own case follows:

A white man aged 34 was seen on Jan. 9, 1940, complaining of blurred vision and of seeing a series of halos around lights and double telephone poles. He said that he was unable to read, but when tested he could see small print if it was held close to the eyes.

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15. Lagrange, H., and Laudat, M.: Transitory Spasmodic Myopia as Sequel of Medication with Sulfanilamide Preparation, Bull. et mém. Soc. méd. d. hôp. de Paris **55**:883, 1939.

16. Heinonen, O.: Transitory Myopia After Use of Sulfanilamide, Duodecim **55**:552, 1939.

17. Fänge, G.: Transitory Myopia Developing After Therapy of Pneumonia with Sulfapyridine, Svenska läk.-tidning. **36**:1197, 1939.

Vision was normal when he retired the night previously, the visual change being noted on arising the next morning.

His general health had been good with the exception of a series of boils, for which a physician had prescribed sulfanilamide. He had taken 5 grains (0.32 Gm.) every two hours for three days, and then stopped for four days. The infection seemed to get worse, with a red streak extending up his arm from the hand, the site of the boils. He did not see his physician during this time but of his own accord resumed the medication in the same manner; at the end of the second day, having ingested about 120 grains (7.77 Gm.), the visual trouble began. The patient had been wearing —0.75 sphere on the right eye and a —0.50 sphere on the left eye previous to this time.

When the patient was seen at the office he was pale, his lips were darkened and he was somewhat apprehensive. Examination showed vision of 20/200 in the right eye; with a —2.50 sphere it increased to 20/20; vision in the left eye was 20/100, and a —3.00 sphere was required for normal sight.

The red glass muscle test showed no marked imbalance. The pupils were round and equal, being very mobile in reacting to light. The conjunctivas were clear. Tension of the eyes was within normal limits. Slit lamp examination revealed nothing unusual. Ophthalmoscopic examination revealed normal fundi, vessels and disks. Examination of the urine gave negative results. Slight anemia was present.

The administration of sulfanilamide was immediately stopped, and the patient was seen on the following day. Examination showed vision of 20/100 in the right eye, which was brought to normal with a —1.00 sphere, and 20/100 in the left eye, with a —1.50 sphere for 20/20 vision. The blurring and other complaints had diminished at this time.

When the patient was seen on January 13, four days after the administration of the drug was stopped, the eyes felt normal and the vision with his regular lens was 20/20 for each eye.

COMMENT

These interesting cases of transitory myopia resolve themselves into a complex problem. Did the myopia occur on the basis of the various infections, was it caused by the ingestion of the drug or did it just happen to take place?

The literature gives descriptions of transitory myopia in connection with a number of general diseases, such as influenza, diarrheal conditions, icterus, acute inflammatory renal diseases and acute polyarthritis. Reports of it also occur in connection with the administration of arsenicals and in connection with alkalinity therapy, according to Sippy.

This type of condition has been reported, independent of any known general symptoms, and it also has been known to occur in connection with diabetes mellitus. In cases of untreated diabetes mellitus it makes its appearance with the excretion of large quantities of sugar.

The cases reported in this paper show the condition taking place in connection with furuncles, pneumonia, sore throat and gonorrhea. These conditions with so varied a reaction practically rule out by themselves the possibility that the disease per se could be the basis for the

myopia. The probability of a disturbed sugar or salt metabolism with changes in the water balance could be considered, but unfortunately no such laboratory work was done. From the work of Mengel [18] it is known that the vitreous and aqueous show a concentration of sulfanilamide of 1.5 to 3.2 mg. per hundred cubic centimeters when it is taken by mouth. In fact, the drug was found to be in that concentration in the vitreous thirty-two minutes after administration.

Thus the mechanism of the reaction must of necessity remain a conjecture. Additional laboratory results would be of value, but since they were not complete, one must piece together what is already known.

It is hardly tenable that changes occurred in the muscular coats of the eyeball to change the refraction for such a short time. Lenticular changes would probably be the best basis for an explanation.

It is conceivable that the rapid absorption of the drug can affect a transformation of the salt and water metabolism in the organism and thus make for a change in the lens which would be responsible for the disturbances to the refraction. Credence must be given to the thought of toxic irritation of the parasympathetic fibers of the ciliary muscles.

The interesting fact that in most of the cases the patient first used the drug with impunity, the trouble starting at the next administration, warrants the conclusion that a sensitivity to the drug might be developed. Nitti and Bovet [19] and Hageman and Blake [10] were unable to produce sensitivity in their various experiments.

Despite the difficulty of deciding on the actual mechanism, the rapid onset after taking the drug and the apparent recovery after stoppage of the medicine seem definitely to indict sulfanilamide. However, good prognosis, with no apparent ill after-effects, is reassuring to all concerned.

SUMMARY

A number of interesting cases of transitory myopia have been noted following the administration of sulfanilamide and 1 after the use of sulfapyridine. The condition in all cleared up following discontinuance of the administration of the drug.

Various ideas as to the mechanism of the reaction are noted together with the possibility of drug sensitivity developing. That there is a good prognosis after such a condition occurs is gratifying.

18. Mengel, W. G.: Determination of Sulfanilamide in Aqueous and Vitreous After Conjunctival and Oral Administration, Arch. Ophth. **22**:406 (Sept.) 1939.

19. Nitti, F., and Bovet, D.: Sulfanilamide and Sensitivity, Bull. Soc. chim. biol. **19**:837, 1937.

REGENERATION OF THE AQUEOUS

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Although an extensive literature is available on ocular manometry and tonometry, there are few reports concerning the flow of aqueous humor from an open eye. The earliest reference to the measurement of such a flow was made in 1702 by Hovius,[1] who measured the escape of fluid when the anterior chamber was opened. In more recent years the determination of the actual rate of formation of aqueous humor has been attempted by numerous workers. The methods of investigation have given rise to two opposing schools. Leber [2] and his followers employed a filtration manometer, by which means the pressure in the eye was kept at a constant level. Any increase in the aqueous humor then forced an equal amount of fluid into a graduated outlet tube. These investigators obtained the following values: [3]

Subject	Amount of Aqueous, Cu. Mm. per Minute	Investigator
Man	5.0	Leber and Bentzen
Rabbit	7.0	Niesnamoff
Rabbit	6.0	Bentzen
Pig	7.0	Niesnamoff
Dog	11.0	Niesnamoff
Cat	24.0	Niesnamoff
Sheep	28.0	Niesnamoff
Cattle	62.0	Niesnamoff

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1. Hovius, J.: De circulari humorum motu in oculo, Traj. ad Rhenum, G. van de Water, 1702; cited by Duke-Elder.[5]

2. Leber, T.: Sur la filtration de l'oeil et sur son rôle dans la pathogénie du glaucome. Remarques relatives au travail de M. le Dr. Uribe y Troncoso, Ann. d'ocul. **133**:401-412, 1905; Encore quelques mots à propos de la mensuration de la filtration de l'oeil, ibid. **134**:217, 1905; Nouvelles recherches sur la pression et la filtration de l'oeil. A propos des questions soulevées par M. Uribe y Troncoso, ibid. **135**:270, 1906.

3. Weiss, O.: Physiologie der Ernährung und der Zirkulation des Auges, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1932, vol. 2, pp. 1-80.

The conclusions of Leber and his students have been opposed by Weiss,[3] Troncoso [4] and others, who have pointed out certain inaccuracies of this method. Troncoso collected the fluid escaping through the anterior ciliary veins which drain Schlemm's canal. After opening these veins, he immersed the subluxated eye into an oil bath. The accumulated fluid was centrifuged and compared with a sample of blood drawn from a vein in the ear. The difference in quantities of the supernatant liquids was due presumably to the aqueous humor. By this method the flow of fluid was found to range from 3 to 9 cu. mm. per minute. Wide variations in values have been reported by writers even in the same animal. Thus, for the rabbit Bentzen [5] and Niesnamoff [6] found the formation to be 6 and 7.0 cu. mm. per minute respectively, while Jesner [7] showed 44 cu. mm. to be formed per minute. Duke-Elder [8] sharply criticized the results of all these investigators because the technics employed in securing these data were unsound physiologically. He therefore believed the value of the determinations to be questionable.

Although the exact measurement of the rate of aqueous formation is attended with great difficulties, the determination of the amount of aqueous drained through a cannula is relatively simple. So far as we can determine there are no data on the flow of aqueous collected by this means under a variety of conditions, such as have been accumulated on intraocular pressure. One possible explanation for the lack of such reports is the questionable significance of the values obtained under the abnormal conditions produced by the experiment. This method, although admittedly unphysiologic, should nevertheless yield information concerning the maximum regeneration of aqueous. Another major obstacle in studies of this nature has been the marked clotting tendency of the plasmoid aqueous. Adamük [9] was the first to notice the presence

4. Uribe y Troncoso, M.: Neue Untersuchungen über die Saftströmung im lebenden Auge und in anderen Organen und ihre Messung, Klin. Monatsbl. f. Augenh. **53**:1-29, 1914.

5. Bentzen, C. F.: Ueber experimentelles Glaukom beim Kaninchen und über die Bedeutung des Kammerwinkel für den intraocularen Druck, Arch. f. Ophth. **41**:42-114, 1895.

6. Niesnamoff, E.: Ueber die quantitativen Verhältnisse der Filtration und Secretion des Kammerwassers, Arch. f. Ophth. **42**:1-35, 1896.

7. Jesner: Der Humor aqueous des Auges in seinem Beziehungen zu Blutdruck und Nervenreizung, Arch. f. d. ges. Physiol. **23**:14-44, 1880.

8. Duke-Elder, W. S.: The Nature of the Intraocular Fluids, British Journal of Ophthalmology, Monograph Supplement III, London, George Pulman & Sons, Ltd., 1927.

9. Adamük, E.: Neue Versuche über den Einfluss des Sympathicus und Trigeminus auf Druck und Filtration in Auge, Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturw. Cl., 1869, vol. 59, pt. 2; cited by Bauer.[10]

of fibrin in the regenerated aqueous, and Bauer [10] observed its coagulability. These observations have been repeatedly confirmed by subsequent workers. This difficulty has been overcome satisfactorily by the intravenous administration of a diffusible anticoagulant, as will be described in the experimental procedure.

EXPERIMENTAL WORK AND RESULTS

It was first necessary to determine the normal rate of aqueous flow from a cannulized eye. For this purpose, dogs were placed under pentobarbital anesthesia, and the blood pressure was recorded by the usual method from the femoral artery. A 27 gage needle was then inserted into the anterior chamber at the most dependent part of the limbus and the aqueous humor aspirated. Immediately after this, a cannula composed of the shaft of an 18 gage needle was passed through the same tract (care being taken to avoid injury to the iris). The beveled edge faced the cornea, and the posterior surface lay parallel to the anterior surface of the iris. After some experience it was possible to perform this maneuver without loss of fluid. The regenerated aqueous was allowed to flow into tubes of known weights which were changed at specified intervals. The original and the plasmoid aqueous were weighed immediately. In our early experiments great difficulty was encountered due to clotting of the aqueous. This manifestation began almost immediately and reached such a degree within thirty minutes that the cannula became obturated. Complete emptying of the chamber was prevented, and no accurate estimation of the flow was possible.

It occurred to us that an anticoagulant introduced into the blood stream should diffuse into the aqueous humor and prevent its clotting. Chlorazol fast pink, an azo dye, was found to act in this manner. This dye was given in a concentration of 60 mg. per kilogram of body weight. Because of its tendency to produce a transient fall in blood pressure, the injection was made fifteen to thirty minutes before paracentesis. The blood pressure returned to the normal level within this period. A single administration of the dye was found to remain effective for two to four hours. Longer experiments usually required further injections. Coagulation of the plasmoid fluid could be anticipated by the decreased coloring of the aqueous. The marked permeability of this dye was evidenced by the rapid staining of the tissues. This was particularly noticeable in the conjunctiva and other mucous membranes, which assumed the pink color of the dye in less than a

10. Bauer, H.: Ueber die Ursache der verändertem Zusammensetzung des Humor aqueous nach Entleerung der vorderen Augenkammer, Arch. f. Ophth. **42**:193-213, 1896.

minute after its intravenous injection. In an unirritated eye the original aqueous humor remained colorless.

Immediately after paracentesis the dye became visible on the anterior surface of the iris, coloring the aqueous humor. This observation was in accordance with the findings of Collins [11] and Seidel,[12] who showed that the plasmoid aqueous originated from the anterior surface of the iris. The aqueous assumed a burgundy color, gradually fading to pale pink unless the dye was replenished. One shortcoming in the use of an anticoagulant was the tendency for greater bleeding when the iris was accidentally injured. It was found, however, that in most of these instances the hemorrhage ceased within thirty minutes and the continuous flow of the aqueous flushed the blood from the anterior chamber, allowing the experiment to be resumed.

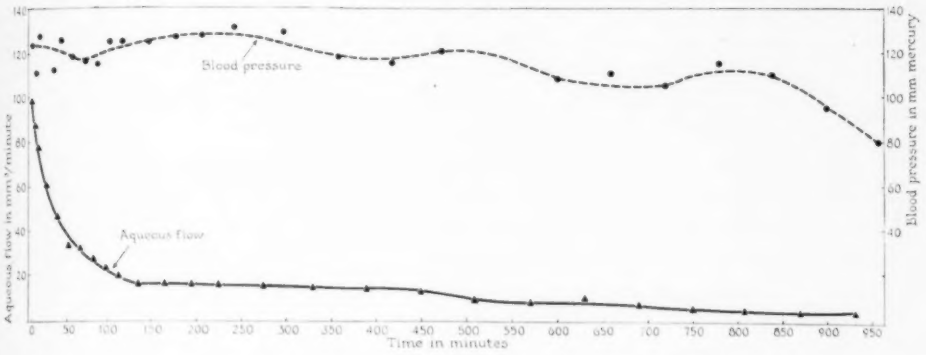

Chart 1.—Average rate of aqueous flow from normal eyes.

The quantity of liquid that drained from the anterior chamber from two and a half minutes to sixteen hours is presented in chart 1. The time plotted on the curve represents the midpoint between successive readings. Even when the blood pressure remained uniform, the rate of flow changed so that three phases can be seen. The first phase consisted of a rapid flow, with the rate dropping precipitously for approximately two hours. Then a relatively constant level was reached and maintained for three to five hours. Finally, a gradual diminution

11. Collins, E. T.: An Experimental Investigation as to Some of the Effects of Hypotony in Rabbits' Eyes, Tr. Ophth. Soc. U. Kingdom **38**:217-227, 1918.

12. Seidel, E.: Ueber die Beteiligung der Iris bei der Kammerwasserabsonderung nach gemeinschaftlich mit Th.-Leber angestellten Versuchen, Ber. ü. d. Versamml. d. ophth. Gesellsch. **40**:431-441, 1916; cited by Seidel, E.: Experimentelle Untersuchungen über Quelle und Verlauf der intraokularen Saftströmung, Arch. f. Ophth. **95**:1-72, 1918.

occurred which appeared to approach zero asymptomatically. The significance of these observations will be discussed later.

There was little correlation between the size of the animal and the volume of the original aqueous humor obtained. In 150 eyes of dogs of varying sizes the amount of aqueous humor ranged from 0.31 to 1.07 cc., with an average value of 0.62 cc. Weiss found the values to be between 0.43 and 0.85 cc., and Golowin,[13] between 0.8 and 1.0 cc.; Niesnamoff reported an average of 0.85 cc. Not only the volume of the original chamber but the rate of aqueous flow was relatively independent of the size of the dog. Many small dogs (5 to 6 Kg.) were found to have a flow considerably more rapid than dogs several times larger.

On the basis of the work by Kronfeld and Lin [14] on the regeneration of aqueous humor in man, it seemed possible that there might be a close relation between the volume of the anterior chamber and the rate of aqueous production. Our data, however, failed to show such a correlation. The difficulties encountered in completely removing all aqueous from the eye have been emphasized by Duke-Elder [8] and may explain the apparent discrepancy.

Adamük was the first to show that the plasmoid aqueous was far richer in proteins than the original fluid. Duke-Elder [8] demonstrated that this increase in colloids was in proportion to the extent of evacuation of the anterior chamber. The methods used for the estimation of the proteins were both physical and chemical. Among the physical methods were those depending on viscosity, conductivity, osmotic pressure, surface tension and index of refraction. The only chemical method employed was the precipitation by acids and subsequent nephelometric estimation. (A complete bibliography appears in Duke-Elder's paper.[8]) In our work changes in the concentration of protein were demonstrated by variations in the specific gravity, the falling drop method of Barbour and Hamilton [15] being used. That the specific gravity of regenerated aqueous humor is higher than that of the original aqueous has already been shown by Golowin. After paracentesis there occurred in each instance a rapid increase in the specific gravity of the aqueous, the peak being reached in between five and twenty-five minutes. This is in agreement with Wessely,[16] who found the maximum concen-

13. Golowin, S. S.: Untersuchungen über das specifische Gewicht des Kammerwasser, Arch. f. Ophth. **49**:27-35, 1900.

14. Kronfeld, P. C., and Lin, C. K.: Further Studies on the Regeneration of the Aqueous in Man, Proc. Soc. Exper. Biol. & Med. **39**:259-267, 1938.

15. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, J. Biol. Chem. **69**:625-640, 1926.

16. Wessely, K.: Experimentelle Untersuchungen über den Augendrucke sowie über qualitative und quantitative Beeinflussung des intraoculären Flüssigkeitswechsels, Arch. f. Augenh. **60**:97-160, 1908.

tration to be attained in thirty minutes, and with Mestrezat and Magitot [17] who found the greatest concentration of protein forty-five minutes after paracentesis. As can be seen in chart 2, an appreciable fall of varying duration followed the rise in each instance. This rise and fall in some animals recurred several times with diminishing intensity, suggesting a rhythm. This is interesting in view of the rhythmic changes in the intraocular pressure manifested by the eye after paracentesis.[18] A possible explanation of this phenomenon is offered in our comment.

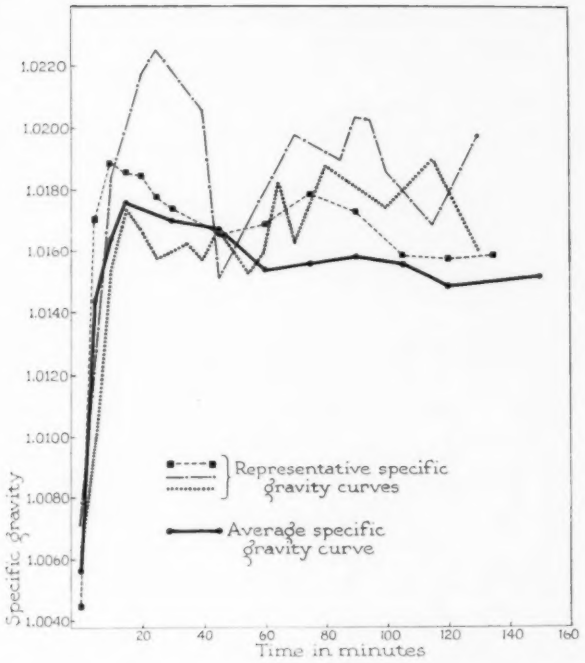

Chart 2.—Variations in the specific gravity of aqueous humor draining continuously from an open eye.

Under the conditions of our experiment (i. e., the insertion of a cannula into the eye) the intraocular pressure is equal to that of atmospheric pressure. This would cause the quantity of fluid escaping from the blood vessels to vary with the height of the blood pressure. Although clinically a close relation between blood pressure and intra-

17. Metrezat, W., and Magitot, A.: Nature de l'humeur aqueuse de seconde formation chez l'homme et l'animal, Ann. d'ocul. **159**:401-415, 1922.

18. Poos, F.: Uveale Gefässreaktionen und Augendruck, Klin. Monatsbl. f. Augenh. **101**:210-221, 1938.

ocular pressure does not exist, in the laboratory animal fluctuations in the former produce similar changes in the latter. Henderson and Starling [19] found that obstruction of the abdominal aorta and injection of nicotine produced an increased intraocular pressure, corresponding with the rise in blood pressure. Other workers [20] have shown similar rises to follow the administration of pitressin and epinephrine. Conversely, administration of histamine, amyl nitrite and acetylcholine resulted in decreased intraocular pressure. A series of experiments were performed to determine whether a similar parallelism existed between the flow of aqueous and the arterial blood pressure. In general, such a correlation was found to obtain. This was consistently observed under

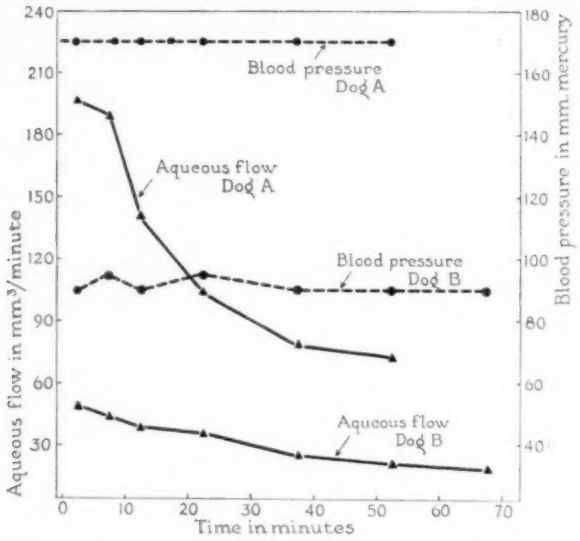

Chart 3.—Rate of aqueous flow from dogs with spontaneously high (*A*) and low (*B*) blood pressures.

a variety of conditions. Thus, otherwise normal animals with a low blood pressure had a slower rate of flow than animals with a high blood pressure. This can be seen clearly from chart 3, in which the flow of aqueous of a typical hypotensive dog is compared with that of a hypertensive dog. The effects of lowering or raising the blood pressure by means of drugs are subsequently described.

19. Henderson, E. E., and Starling, E. H.: The Influences of Changes in the Intraocular Circulation on the Intraocular Pressure, J. Physiol. **31**:305-319, 1904.

20. Colle, J.; Duke-Elder, P. M., and Duke-Elder, W. S.: Studies on the Intraocular Pressure: I. The Action of Drugs on the Vascular and Muscular Factors Controlling the Intraocular Pressure, J. Physiol. **71**:1-30, 1931.

Effect of Decreasing Blood Pressure.—It was repeatedly observed that a marked decrease in the blood pressure for any reason whatever was almost invariably followed by an abnormal slowing of the flow of aqueous. Chart 4 shows the sudden diminution following the intravenous injection of 0.2 cc. of a 1:1,000 concentration of histamine dihydrochloride. It can be noted that for the five minutes during which the blood pressure remained at the extremely low level of 20 mm. of mercury no aqueous was formed. The flow was resumed only after the rise in blood pressure had begun. Another interesting point is apparent from this curve, namely, that the early decrease in the formation of aqueous is so rapid that a slight rise in the blood pressure at this point is an insufficient compensatory mechanism. Hence the amount of

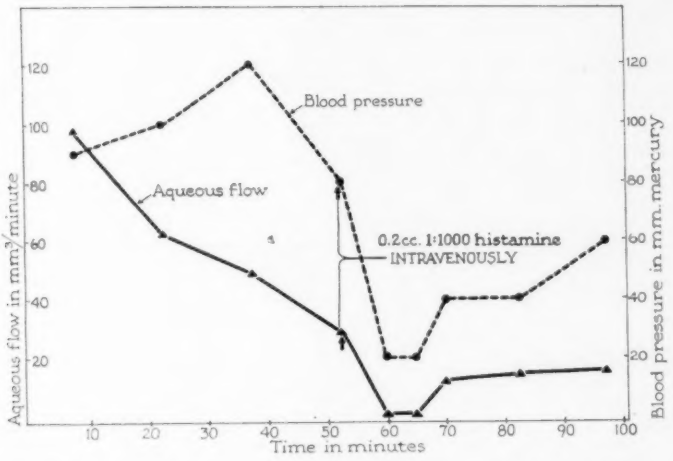

Chart 4.—Effect of histamine injected intravenously on the flow of aqueous.

aqueous formed dropped from 98 cu. mm. per minute to 49 cu. mm. between the seven and a half and thirty-seven and a half minute intervals despite a rise of 30 mm. of mercury in blood pressure during the same period. A similar diminution in the production of aqueous was observed when the blood pressure was lowered by injection of acetylbetamethylcholine chloride, by intravenous injection of lactic acid, by sublingual administration of glyceryl trinitrate and by hemorrhage. Changes in specific gravity also occurred with decreased blood pressure. Chart 5 shows such a change in a dog whose blood pressure fell spontaneously. A value of 1.0091 was reached, whereas the average minimum value had been 1.0149, and values below 1.0120 were rarely seen even in dogs with normally low blood pressures.

Effects of Increasing the Blood Pressure.—Although it is a simple matter to produce and maintain a low blood pressure, it is a more difficult task to obtain a sustained rise in blood pressure. Because of the inherent shortcoming of our method, namely, inability to detect slight transient alterations in the flow, only those substances that cause a marked rise or a relatively sustained rise gave unequivocal results. Of the former group, nicotine was the best representative; of the latter, pitressin. The intravenous injection of 0.2 cc. of a 1 per cent solution of nicotine, as indicated in chart 6, caused an immediate increase of the blood pressure from 60 to 250 mm. of mercury and of the aqueous flow from 30 to 125 cu. mm. per minute. Five minutes after the peak had been reached, the blood pressure dropped to 40 mm. of mercury and the formation of aqueous showed an equally precipitous decline.

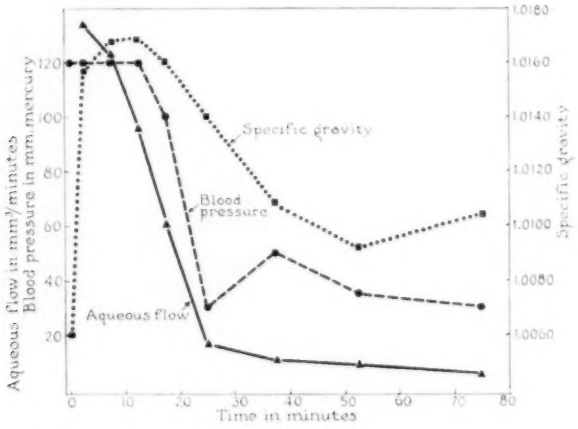

Chart 5.—Effect of a fall in blood pressure on the specific gravity and flow of aqueous humor.

After the injection of 0.3 cc. of pitressin (6 pressor units) the blood pressure rose from 40 to 110 mm. of mercury and was maintained at this level for ten minutes. During this time the flow of aqueous could be seen to increase (chart 7). With the return of the blood pressure to the previous level, the flow again was decreased markedly.

Attempts to increase the flow of aqueous by intravenous injection of epinephrine were inconclusive. This may have been due to the fleeting rise produced by this drug or to certain local circulatory alterations which counterbalanced the systemic rise. The latter explanation is in agreement with the findings of Duke-Elder and co-workers, who observed a rise in intraocular pressure with small amounts of epinephrine

20. Footnote deleted on proof.

(in which the rise of the systemic blood pressure predominates), whereas with larger amounts a decreased intraocular pressure was noticed (presumably due to local vasoconstriction).

The dependence of the flow of aqueous on systemic arterial blood pressure can best be shown by alternately lowering and raising the blood pressure of the same dog. The results of such an experiment are shown graphically in chart 8. A male dog weighing 9.1 Kg. and having a blood pressure of 120 mm. of mercury was used. Two hundred cubic centimeters of blood was withdrawn from the femoral artery before paracentesis of the cornea. The blood pressure dropped to 40 mm. of

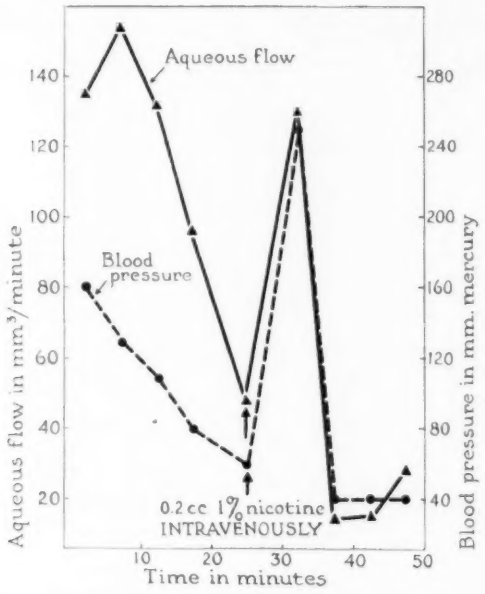

Chart 6.—Effect of nicotine injected intravenously on the flow of aqueous.

mercury and remained at this level for fifteen minutes. Four hundred cubic centimeters of isotonic saline solution was then given intravenously, causing a rise in blood pressure to the original level within thirty minutes. The procedure was repeated (bleeding and intravenous injection), and, as can be seen from chart 8, the flow of aqueous followed closely the blood pressure. It will be further noted that during the fifteen minute interval immediately after paracentesis the flow was slow, whereas ordinarily it was profuse at this time. When the blood pressure was raised, the flow immediately increased. The fall and rise recurred with a diminished intensity after a second bleeding and injection respectively.

Under normal conditions, the dye appears immediately after paracentesis. In the instance in which the blood pressure was 40 mm. of mercury at the time of paracentesis no dye could be observed in either eye until the blood pressure reached a level of 60 mm. of mercury, a

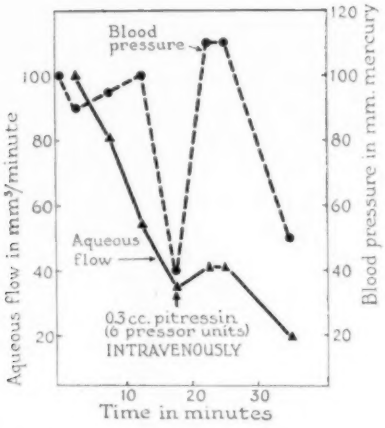

Chart 7.—Effect of pitressin injected intravenously on the flow of aqueous.

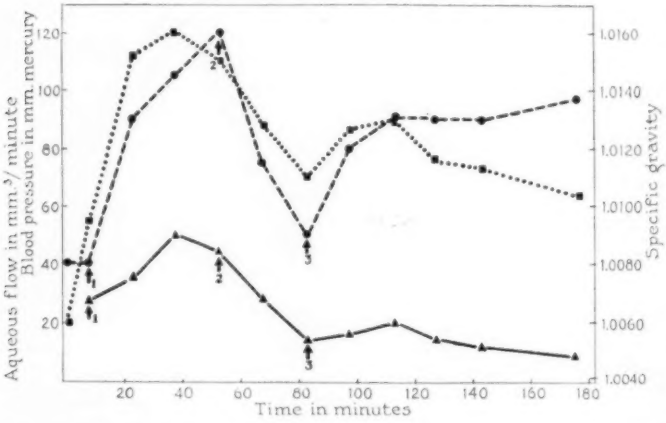

Chart 8.—Effect of variations in blood pressure on the specific gravity and flow of aqueous humor. The blood pressure of the animal was reduced by bleeding prior to paracentesis. At *1*, 400 cc. of isotonic saline solution was injected intravenously; at *2*, 200 cc. of blood was removed, and at *3*, the injection of 400 cc. of isotonic saline solution was repeated.

matter of twenty minutes after paracentesis. In harmony with this observation were the findings relating to specific gravity. The values remained extremely low until the blood pressure rose. Thus, the specific

gravity of the regenerated aqueous for the first fifteen minutes was 1.0095, a value not appreciably higher than that of the original aqueous (1.0080), whereas with normal blood pressure the specific gravity at this time was usually at a maximum (1.015 to 1.023). When the blood pressure was raised, the specific gravity attained a value of 1.0161. With the repetition of the experiment, the specific gravity of the liquid fell and rose with the blood pressure.

The ocular ischemia produced by marked diminution in blood pressure can be simulated by the interruption of the blood supply. This was performed by alternately clamping and releasing the carotid artery. Chart 9 demonstrates the close dependence of the flow of aqueous on the blood supply to the eye.

Effect of Drugs Injected Locally.—As already stated, epinephrine injected into the general circulation produced a variable effect on the eye,

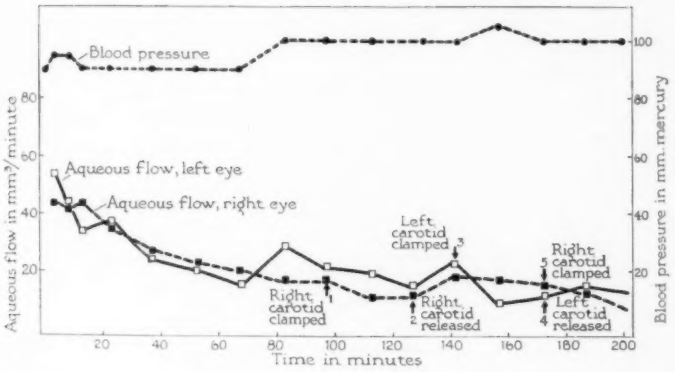

Chart 9.—Effect on the flow of aqueous of alternately clamping and releasing the carotid artery.

depending on whether the general systemic rise in the arterial pressure was sufficiently great to overcome the ocular vasoconstriction or, conversely, whether the latter condition was so marked as to counterbalance the effect of the former. It has been reported that if the effect is localized on the capillaries of the eye, as by subconjunctival or intraocular injection of the drug, a decrease in intraocular pressure results.[21] In our attempts to repeat this work, using the rate of aqueous flow as an indication of alteration in the capillary permeability, we found no change on subconjunctival injection of a 1:1,000 concentration of epinephrine

21. Rubert, J.: Ueber den Einfluss des Adrenalins auf den intraokularen Druck, Ztschr. f. Augenh. **21**:97-115, 1909. Erdmann, P.: Ueber die Wirkung fortgesetzter subkonjunktivaler Injektionen von Nebennierenpräparaten beim Kaninchen und ihre therapeutische Verwendung beim Menschen, ibid. **32**:216-225, 1914.

hydrochloride. This may have been due to the minute quantities which actually reached the intraocular vessels. Apparently this is sufficient to cause changes detectable by manometric or tonometric means but inadequate to produce a noticeable alteration of the flow of aqueous. The ineffectiveness of subconjunctival injections and surface applications was likewise observed with most other drugs. Therefore, in the subsequent experiments retrobulbar injections were regularly employed, with the following results.

Effect of Drugs Injected Retrobulbarly.—Epinephrine Hydrochloride: A marked reduction in the quantity of aqueous flow was apparent when 0.25 cc. of a 1:1,000 concentration of epinephrine hydrochloride was administered retrobulbarly. The drug was given two minutes before

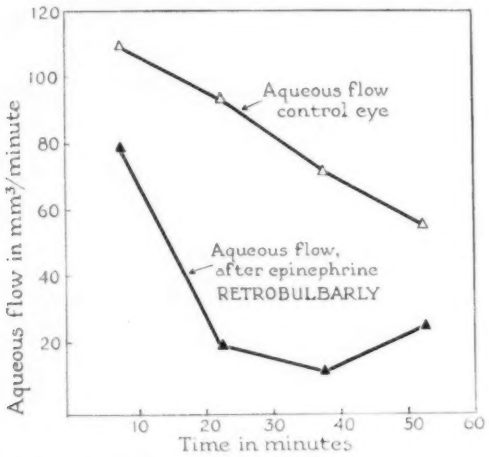

Chart 10.—Effect of epinephrine injected retrobulbarly on the flow of aqueous.

paracentesis and caused only a slight decrease in the first fifteen minutes as compared to the control eye in which an equal quantity of saline solution was injected. The most marked effect occurred during the second fifteen minute interval. The drop persisted for forty-five minutes and was followed by a slight rise (chart 10). The rise in specific gravity was considerably delayed, the maximum concentration being attained after forty-five minutes, whereas in the control eye the peak was reached within fifteen minutes.

Atropine Sulfate: Atropine sulfate (0.04 mg. in 0.2 cc. of saline solution) was injected retrobulbarly two to six minutes before paracentesis of the eye. A similar quantity of saline solution was injected in the control side. Chart 11 shows a typical response. It will be noted that the formation of aqueous was appreciably decreased by the drug. The

maximum effect appeared after fifteen to thirty minutes. Because of this delayed action, certain variations were found. Hence, in several experiments no decrease occurred (compared to the control eye) until this time was reached. In other dogs the difference between the two eyes gradually increased, reaching a maximum at this time.

Histamine Dihydrochloride: The effect of histamine on the flow of aqueous varied considerably from dog to dog. The general statement seems justified that histamine dihydrochloride (0.1 cc. of a 1:1,000 concentration) given retrobulbarly prior to paracentesis causes an increased flow of aqueous. With histamine administered after paracentesis, the flow in some instances was increased and in other cases actually decreased. No conclusions could be drawn from the results obtained when histamine was applied locally or subconjunctivally except

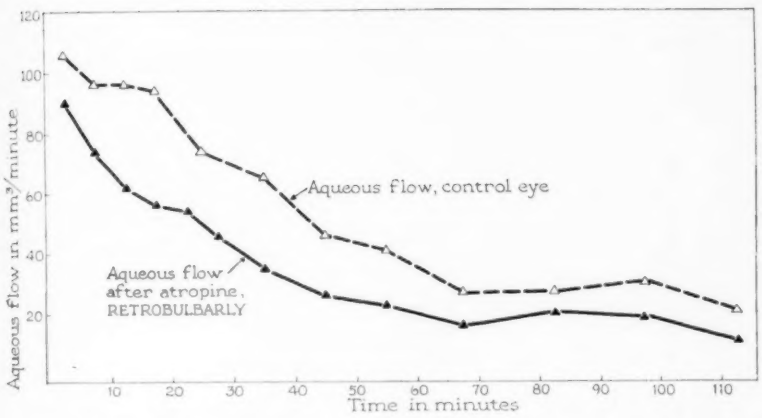

Chart 11.—Effect of atropine injected retrobulbarly on the flow of aqueous.

that the dye could be seen more rapidly in the conjunctiva than normally, suggesting an increased permeability. Injection directly into the anterior chamber some time after drainage had begun resulted in an increased flow (compared to that of the control eye).

Acetylbetamethylcholine Chloride (Mecholyl Chloride): The retrobulbar injection of mecholyl chloride in doses of 0.75 to 1 mg. gave rise to an interesting series of reactions which could be largely predicted from our previous experiments (chart 12). The marked vasodilatation produced by the drug caused a drop in blood pressure of 60 to 70 mm. of mercury within thirty seconds, even when it was injected into the orbit. Such a sharp drop would ordinarily cause a further decrease in the production of aqueous. This was actually observed with the control eye (isotonic saline solution introduced retrobulbarly).

However, the production of aqueous from the eye stimulated by mecholyl chloride increased during this period. As the blood pressure rose, the production of aqueous in the control eye gradually increased and that in the eye receiving mecholyl chloride decreased. A second injection of the drug caused a less marked fall in blood pressure, so that the local action was less complicated by systemic effects. After this injection, therefore, the production of aqueous rose sharply in the eye receiving mecholyl chloride. The slight increase observed in the other eye will be discussed in a later section.

Physostigmine Salicylate: Physostigmine salicylate, as was expected, produced results similar to mecholyl chloride (chart 13). When 0.04 mg. (0.2 cc.) was given retrobulbarly the flow of aqueous

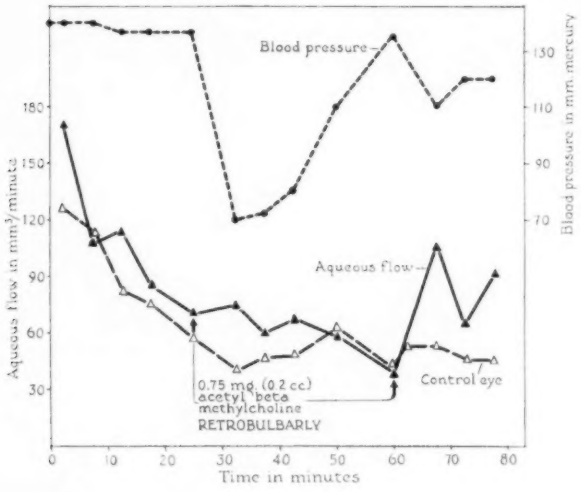

Chart 12.—Effect of mecholyl chloride injected retrobulbarly on the flow of aqueous.

was significantly increased. Since it had less effect on the blood pressure than mecholyl chloride, the local action of the drug was more manifest. As with mecholyl chloride, a subsequent increase in the flow from the control eye was observed. This, too, was probably induced by the drug reaching the other eye through the general circulation. That physostigmine salicylate was absorbed into the general circulation was evidenced by the salivation consistently observed.

Prostigmine Methylsulfate: The action of prostigmine methylsulfate was similar to, but less marked than, that of physostigmine salicylate, as manifested by the slight and transitory increase of the flow of aqueous when 0.5 cc. of a 1:2,000 solution was given retrobulbarly.

Procaine Hydrochloride: Because of the widespread use of procaine hydrochloride in ophthalmology, its action on the flow was investigated. Entirely negative results were obtained following the retrobulbar injection of 1 cc. of a 4 per cent solution.

Ergotamine Tartrate (Gynergen): Ergotamine tartrate has been used to reduce the intraocular pressure in glaucoma.[22] The action, if any, on the flow of aqueous on the retrobulbar injection of 0.5 cc. (0.25 mg.) of this drug was insufficient to be detected by our method.

Effect of Secretin[23] *and Urogastrone*[24].—Since Robertson's work suggested that the secretion of aqueous may be related to other secretions (notably gastric), it was of interest to determine the action of a secretory stimulant and inhibitor respectively. The secretin employed was a highly

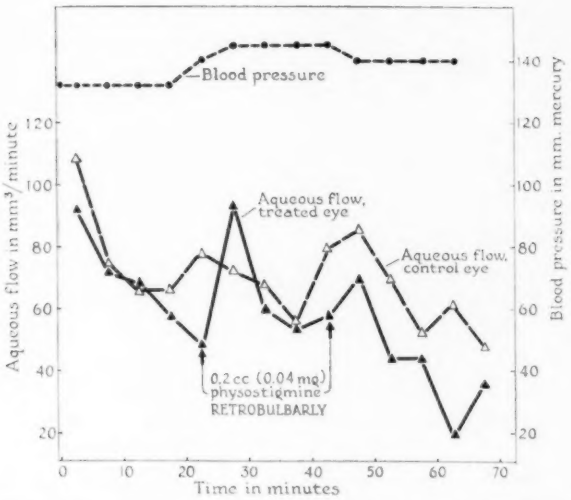

Chart 13.—Effect of physostigmine salicylate injected retrobulbarly on the flow of aqueous.

purified preparation of proved effectiveness. The urogastrone was isolated from the urine of normal persons and was shown to decrease gastric secretion of dogs markedly. After intravenous injection both substances were completely ineffective in altering the flow of aqueous.

Finally, to complete the study of the flow of aqueous the effect of heat, local irritants and the intravenous injection of salt solution were investigated.

22. Heim, H.: Zur Behandlung des Glaukoms mit Ergotamin, Klin. Monatsbl. f. Augenh. **79**:345-351, 1927. Werner, S.: Ueber die Einwirkung subkutaner Gynergen (Ergotamin) Injektionen auf den Druck bei Glaukom, Acta ophth. **9**:275-301, 1931.

23. Supplied by Dr. H. Greengard.

24. Supplied by Dr. J. S. Gray.

Effect of Heat.—Because of technical difficulties, the local application of heat was not investigated. However, a systemic rise in temperature was produced by means of an electromagnetic generator. The drop in the flow of aqueous that occurred normally was less marked as the body temperature rose.

Effect of Salt Solutions Injected Intravenously.—Given separately hypotonic, isotonic and hypertonic solutions showed no consistent effect on the flow of aqueous when the blood pressure was constant. However, when an isotonic solution was followed by a hypertonic solution a moderate increase of flow was observed. The following is a typical experiment:

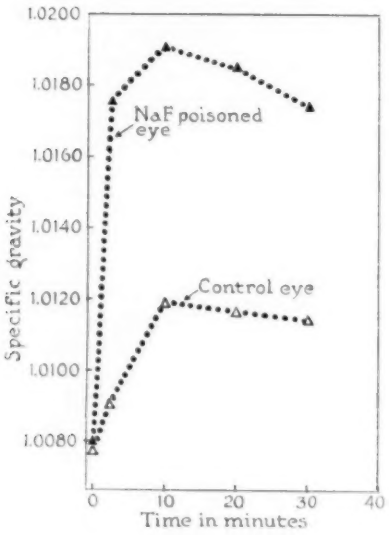

Chart 14.—Effect of sodium fluoride injected intraocularly on the specific gravity of aqueous.

Dog 71, a male, weighing 11 Kg., was given 150 cc. of isotonic saline solution intravenously during a ten minute interval. A slight rise in aqueous flow was noticed (44 to 52 cu. mm.) within twenty minutes after injection. At this time 20 cc. of a 30 per cent salt solution was injected, causing the flow to increase within ten minutes (to 76 cu. mm. per minute). This value dropped to 22 cu. mm. per minute within forty minutes. A further injection of 50 cc. of a 10 per cent salt solution occasioned a second rise to 28 cu. mm. per minute within twenty minutes.

Effect of Local Irritants.—Attempts were made to increase the local flow of blood by retrobulbar injections of irritants. Ether, benzene and turpentine, when injected into the retrobulbar tissues, caused no change

in the flow of aqueous, except in a single instance when 0.5 cc. of benzene thus injected produced a marked increase, which persisted for more than an hour.

The intraocular injection of sodium fluoride produced noteworthy changes. Two milligrams of sodium fluoride in 0.2 cc. of saline solution was introduced into the vitreous humor eighty-five minutes before paracentesis. An equal amount of physiologic solution of sodium chloride was injected into the other eye. At the time of the paracentesis the poisoned eye displayed typical signs of iridocyclitis (i. e., deep chamber, miosis and indistinct iris markings). It was further noted that the aqueous was colored by the dye, whereas that of the control eye remained colorless. This observation pointed to an increased capillary permeability. Determinations of the specific gravity confirmed this (chart 14). In spite of the increased capillary permeability, the rate of flow was not increased.

COMMENT

The cause of the rapid fall in the rate of production of aqueous when it is being constantly removed is difficult to explain. No single explanation seems adequate. That the drop is not due to changes in the systemic blood pressure is obvious, since the decrease in flow occurs even with normal or rising blood pressures. Stagnation, edema or other alterations in the local vascular system may conceivably contribute to such a change. It seems unlikely, however, that changes in the constriction of the capillaries play an important role. This is borne out by the observation that the specific gravity, which varied directly with the state of capillary permeability, rose during the period when the diminution in flow was greatest.

Another explanation is based on the hypothesis (Duke-Elder [8]) that the plasmoid aqueous is a true secretion. On this assumption it may be argued that the rapid drop was caused by an exhaustion of the secretory cells. However, from the close similarity of plasmoid aqueous to the blood, it is believed by most investigators that the former is not a secretion but a transudate.

Finally, this decrease in flow may be explained by the protrusion of the lens into the pupil due to the reduced pressure in the anterior chamber. This would produce a ball valve effect, so that as the pressure increases in the posterior chamber the obstruction of the flow into the anterior chamber becomes greater. If the aqueous flow is the sum of that arising from the ciliary body and that from the iris, this last theory might offer an explanation for the relative constancy of the flow which follows the original sharp decline. The ball valve action would dam back the aqueous from the ciliary body, not only preventing its passage into the anterior chamber, but decreasing its formation due to the back

pressure. Therefore, the flow observed during this period would be from the iris alone. In time the pressure might become so great that the vessels of the iris itself would become constricted, decreasing further the flow. This would correspond with the final gradual diminution of the flow noted in chart 1. Further support of this explanation was the observation that following a puncture of the vitreous the flow of aqueous became accelerated. It may be assumed that the decreased pressure following posterior sclerotomy permitted the lens to resume a more normal position in relation to the iris, which permitted the escape of fluid into the anterior chamber through the pupil. Finally, the repeated observations that a stimulus was most effective during the early part of the experiment would be additional support of this explanation. For example, in the earlier stages of the experiment the marked increase of flow with a rise in blood pressure would be due to the greater freedom of egress of fluid. This is in contrast with the small increase in the later stages, when the valve action of the lens should be most effective.

The rapid rise in specific gravity following paracentesis to a maximum in five to twenty-five minutes is in harmony with the work of Wessely and of Mestrezat and Magitot, who showed that the maximum protein content was reached at thirty and forty-five minutes after paracentesis, respectively. A slight though ill defined rhythmic tendency was also noted. Similarly, a rhythm in intraocular pressure has been reported by Poos. This suggests a variation in the tonus of the capillaries, possibly in an attempt to maintain a normal state. In this connection it was noted that a marked decrease in blood pressure usually was accompanied by a similarly marked decline in the specific gravity. This likewise may be due to vasoconstriction of the capillaries, retarding the colloidal particles. Further evidence of this is the accompanying decrease in coloring of the aqueous with a lowering of blood pressure.

As could be anticipated from tonometric and manometric investigations, the flow of aqueous followed closely variations in the blood pressure. Further discussion of this phase is unnecessary, since considerable literature is already available on the relation of blood pressure to intraocular tension.

With epinephrine, as with the other drugs employed, no significant changes were noted on surface application and subconjunctival injection. This ineffectiveness was probably due to the low concentration reaching the intraocular vessels. Slight changes that might be produced in this manner were too small in magnitude to be detected by our method. Administered retrobulbarly, however, epinephrine manifested its vasoconstrictive action by a sharp decline in the flow of aqueous. The slow rise in specific gravity of the plasmoid aqueous was in agreement with

the findings of Wessely,[25] who demonstrated that a rise in protein in the second aqueous was less than normal if this drug had been administered previously. Clinically, it has been recognized that the effectiveness of epinephrine in lowering the intraocular pressure is greatest between fifteen and thirty minutes after injection.

The diminution of flow on injection of atropine may be explained either on the basis of its well known influence on secretions or its effects on the blood vessels. Adler and Landis [26] expressed the belief that some vasoconstrictive action may be produced by the action of atropine. Most workers, however, claim vasodilatation to result due to stimulation of the vasodilator center. The decreased flow of aqueous despite such a vasodilatation suggests that a secretory mechanism may be active. This is in harmony with the ability of atropine to decrease most secretions (salivary, gastric, pancreatic, sweat, mucus, etc.), which has long been recognized. One cannot, therefore, exclude in the present state of knowledge a similar action on the aqueous.

The role of histamine in the eye is of special interest, since it has been suggested by some investigators as a possible factor in the pathogenesis of glaucoma.[27] Friedenwald [28] has produced experimentally lesions which histologically resembled acute glaucoma by injection of histamine intraocularly. The confused results obtained by us with this drug may be due to its dual action on the peripheral blood vessels, namely, dilatation of the capillaries and constriction of the arterioles. Duke-Elder [27b] has shown a rise in intraocular pressure to result if the vessels possess a normal degree of tonicity. This would be the case when histamine was injected before paracentesis. When the capillaries are atonic (maximally dilated), as after paracentesis, the drug produces no further dilatation. Its action is then limited to a constricting effect on the arterioles, which lowers the intraocular pressure and presumably decreases the flow of aqueous.

The sequence of events resulting from administration of mecholyl chloride can be explained largely on its vasodilating action. This would

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25. Wessely, K.: Ueber die Wirkung des Suprarenins auf das Auge, Ber. ü. d. Versamml. d. ophth. Gesellsch. (1900) **28**:69-83, 1901; cited by Wessely, K.: Zur Wirkung des Adrenalins auf Pupille und Augendruck, Ztschr. f. Augenh. **13**:310-320, 1905.

26. Adler, F. H., and Landis, E. M.: Studies on the Protein Content of Aqueous Humor: The Effects of Miotics and Mydriatics, Arch. Ophth. **54**:265-279, 1925.

27. (*a*) Rycroft, B. W.: The Vascular Control of the Intraocular Pressure: Some Experimental Observations, Tr. Ophth. Soc. U. Kingdom **54**:315-326, 1934. (*b*) Duke-Elder, W. S.: The Metabolism of the Eye: II. Clinical Applications, Arch. Ophth. **6**:158-180 (Aug.) 1931.

28. Friedenwald, J. S.: Pathogenesis of Acute Glaucoma, Arch. Ophth. **3**:560-573 (May) 1930.

give rise to local and systemic changes, which at times might produce contradictory results. Thus, vasodilatation locally caused an increased flow of aqueous which was partly counterbalanced by a simultaneous drop in systemic blood pressure. In the control eye a drop was noted due to the systemic effect, whereas the eye receiving mecholyl chloride showed a slight rise. As the local concentration of the drug became less, the systemic effect predominated even on the side into which injection was made. The control eye showed a later rise, presumably due to the time required for its accumulation in sufficient quantities at this point. A subsequent injection of mecholyl chloride showed a less marked fall in blood pressure, so that the local action predominated and a much greater increase in rate of flow was produced. The action of this drug on a possible secretory phase of aqueous formation cannot be disregarded, in view of its marked stimulation of the gastric secretion.

Physostigmine acts by neutralizing the choline esterase and thus allowing acetylcholine to exert its effect. The pharmacologic actions of acetylcholine are in most respects identical with those of mecholyl chloride, which have already been discussed. The original effect of physostigmine is more marked than that of mecholyl chloride. This can be explained by its less marked effect on the blood pressure, thus allowing the local vasodilatation to become more manifest. As with mecholyl chloride a subsequent increase of aqueous formation in the control eye was observed.

The rise of body temperature produced by diathermy caused the flow of aqueous to be maintained at a relatively rapid rate for a considerable time. This may be explained by the well known vasodilating effect of heat.

It is difficult to interpret the effects produced by the intravenous injection of salt solutions. The consistent rise in flow when the injection of isotonic fluid was followed by the injection of hypertonic solutions is best explained on a basis of an increased blood volume. If this explanation is true, the ineffectiveness of isotonic saline solution alone can be interpreted by assuming a rapid removal from the blood stream. The inability of hypertonic solutions to decrease the flow is not in harmony with the conclusions of Robertson,[29] who expressed the belief that such solutions depress secretory activity of the ciliary body. However, if one assumes the secretion to be but a small part of the total aqueous flow, secretory inhibition might be of insufficient magnitude to be detected by our method.

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29. Robertson, J. D.: An Investigation into the Theories on the Formation and Exit of the Intraocular Fluids, Brit. J. Ophth. **21**:401-448, 1937. Noble, R. L., and Robertson, J. D.: The Effects of Hypertonic Solutions on Gastric Secretion and Intraocular Pressure, J. Physiol. **93**:430-437, 1938.

The effects of the local irritants were not sufficiently noteworthy to merit further discussion than that which has already been included in the experimental section.

In general, then, we have found an increased flow of regenerated aqueous under those conditions which produced increased intraocular pressure and vice versa. This is especially apparent with alterations of the blood pressure. The exceptions noted can almost invariably be explained on the basis of local vasomotor alterations which may at times produce effects contrary to those expected from a consideration of the systemic blood pressure alone.

Although the general and local circulatory effects undoubtedly play an important, and probably a predominant role in the regeneration of the aqueous humor, it is nevertheless difficult to exclude entirely a true secretory action as an added factor. The stimulation and inhibition of aqueous flow by agents known to act similarly on proved secretory organs are highly suggestive. Especially striking in this respect was the effect of atropine, which decreased the flow of aqueous and which is known to decrease numerous secretions. This decrease resulted despite a vasodilating action, which with other drugs regularly produced an increased flow due to a concomitant increase in capillary permeability.

SUMMARY

A method is described whereby aqueous humor may be collected through a cannula for long periods of time without clotting of the plasmoid fluid. This was accomplished by the intravenous injection of chlorazol fast pink, an anticoagulant of blood.

By this method, the flow of regenerated aqueous was determined for intervals ranging from five minutes to sixteen hours. A rapid diminution of the rate of flow was observed for approximately two hours after paracentesis, a comparatively constant flow for the next three to five hours and finally a slow decline until the completion of the experiment. Various explanations for these findings are discussed.

The specific gravity of the aqueous increased sharply after paracentesis and reached a maximum within five to twenty-five minutes. With a low blood pressure, low values for specific gravity were usually obtained.

The flow of aqueous followed directly changes in blood pressure. Lowering of the systemic pressure by hemorrhage, by the administration of glyceryl trinitrate or by intravenous injection of histamine or lactic acid decreased the flow. Conversely, an increase was secured when blood pressure was raised by transfusion or by the injection of nicotine or pitressin.

Clamping the carotid artery decreased the flow of aqueous from the eye supplied by it. Release of the artery produced a resumption of normal flow.

Epinephrine hydrochloride or atropine sulfate injected retrobulbarly decreased the flow of aqueous. The specific gravity of the plasmoid aqueous after injection of epinephrine showed a slower rise after paracentesis than did that from the control eye.

The results with histamine were variable. In general, its retrobulbar injection increased the flow.

Physostigmine salicylate, mecholyl chloride and prostigmine methylsulfate each produced an increased flow when given retrobulbarly. The effectiveness of these drugs were in the order listed.

Procaine hydrochloride, ergotamine tartrate, secretin and urogastrone gave negative results by our method.

Systemic pyrexia delayed the rapid decrease in flow normally obtained.

Hypotonic, isotonic and hypertonic solutions given separately were without action. The injection of isotonic saline solution followed by the injection of hypertonic saline solution increased the flow of aqueous.

Local irritants injected retrobulbarly were ineffective except for a single instance. In this case benzene produced a marked and prolonged stimulation of the flow.

The intraocular injection of sodium fluoride produced an increased capillary permeability, as indicated by the penetration of dye given intravenously and by increased values for specific gravity.

The effects of these drugs and conditions on the flow of aqueous have been discussed on the basis of local and general circulatory changes and the secretory activity of the ciliary body.

Prof. S. R. Gifford and Prof. C. J. Farmer gave advice on this work.

EXPERIMENTAL EXOPHTHALMOS AND ASSOCIATED MYOPATHY INDUCED BY THE THYROTROPIC EXTRACT

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SAN FRANCISCO

A study of malignant exophthalmos has been carried on in this clinic for several years.[1] In addition to the clinical studies, considerable experimental work has been done, the results of which are reported here.

A historical review of the older research and theories on exophthalmos has been presented in detail previously [1] and need not be repeated.

The term malignant exophthalmos is used to designate the progressive proptosis which, in a small group, increases to an alarming extent. It usually occurs after thyroidectomy in the presence of a low basal metabolic rate, and unless it is relieved by operative decompression of the bony orbit, as devised by Naffziger,[1] corneal ulceration, infection and fatal intracranial extension of the orbital cellulitis will develop in a high percentage of the patients. The pathologic changes and immediate cause of the exophthalmos occurring in these patients were described in detail in previous reports.[1] In brief, the extraocular muscles were found to be enlarged from three to eight times. Grossly, the musculature of the orbital muscle cone was observed to be pale, edematous, occasionally gritty to the knife, firm and with much fibrous tissue present. Histologically, various stages of degeneration were observed, with interstitial edema, proliferation of small round cells, which tended to accumulate about blood vessels, and fibrosis, which appeared more dense and extensive in the cases in which the condition was more advanced.

From the Department of Surgery, University of California Medical School.

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Read at the joint meeting of the Section on Ophthalmology and the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. (*a*) Naffziger, H. C.: Progressive Exophthalmos Following Thyroidectomy: Its Pathology and Treatment, Ann. Surg. **94**:582-586 (Oct.) 1931. (*b*) Naffziger, H. C., and Jones, O. W., Jr.: The Surgical Treatment of Progressive Exophthalmos Following Thyroidectomy, J. A. M. A. **99**:638-642 (Aug. 20) 1932. (*c*) Naffziger, H. C.: Pathologic Changes in the Orbit in Progressive Exophthalmos, Arch. Ophth. **9**:1-11 (Jan.) 1933; (*d*) Progressive Exophthalmos Associated with Disorders of the Thyroid Gland, Ann. Surg. **108**:529-544 (Oct.) 1938.

The fact that exophthalmos may occur with hyperthyroidism and yet may steadily progress to a malignant form in the presence of postoperative hypothyroidism has led to speculation as to the etiologic relation between the exophthalmos and the thyroid gland. The association must be more than coincidental, and an indirect relation with hormones affecting the thyroid gland, such as the thyrotropic hormone of the anterior lobe of the pituitary body, is suggested. A review of all cases of malignant exophthalmos in the University of California Hospital strongly suggested a glandular dysfunction in the majority of them, and in many instances the findings were consistent with some disturbance of the hypophysis. Because of the successes recently reported in the experimental production of exophthalmos by the use of whole extracts of the anterior lobe of the pituitary body, the present studies were centered about this method.

Schockaert [2] first observed exophthalmos in young ducks given daily doses of a fresh, centrifuged, saline suspension of the anterior lobe of the pituitary body of cattle. Loeb and Friedman [3] obtained exophthalmos in guinea pigs by using injections of an acid extract of the anterior lobe of the pituitary body of cattle. The exophthalmos receded if the injections were discontinued and disappeared under narcosis, in debilitated states and after death. Marine and Rosen [4] produced exophthalmos in young guinea pigs by the injection intraperitoneally of an extract of the anterior lobe of the pituitary body and observed that hyperplasia of the thyroid was associated with the exophthalmos. They found, however, that exophthalmos developed as readily in thyroidectomized guinea pigs as in those not operated on. Exophthalmos was similarly produced experimentally in guinea pigs by Friedgood [5] by means of daily intraperitoneal injections of extracts of the anterior lobe of the pituitary body. The exophthalmos appeared on the tenth day, when the basal metabolic rate was highest and the thyrotoxicosis was most marked. He observed, however, that the exophthalmos became more marked during a refractory period and was striking when the administration of the extracts was continued several months, especially in those animals in which a low

2. Schockaert, J. A.: Hyperplasia of Thyroid and Exophthalmos from Treatment with Anterior Pituitary in Young Ducks, abstracted, Proc. Soc. Exper. Biol. & Med. **29**:306-308 (Dec.) 1931.

3. Loeb, L., and Friedman, H.: Exophthalmos Produced by Injections of Acid Extract of Anterior Pituitary Gland of Cattle, Proc. Soc. Exper. Biol. & Med. **29**:648-650 (Feb.) 1932.

4. Marine, D., and Rosen, S. H.: Exophthalmos in Thyroidectomized Guinea Pigs by Thyrotropic Substance of Anterior Pituitary and the Mechanism Involved, Proc. Soc. Exper. Biol. & Med. **30**:901-903 (April) 1933.

5. Friedgood, H. B.: Experimental Exophthalmos and Hyperthyroidism in Guinea Pigs, Bull. Johns Hopkins Hosp. **54**:48-74 (Jan.) 1934.

basal metabolic rate developed. In 3 guinea pigs the exophthalmos persisted over long periods, even though the injections were discontinued.

Since the work reported in this paper was undertaken, three other reports have appeared. Smelser [6] administered to guinea pigs daily injections of an extract of the anterior lobe of the pituitary body of cattle over periods of from three to nine weeks. All the animals became thyrotoxic, and in 3 of 26 slight exophthalmos developed. Twenty-six other guinea pigs were subjected to thyroidectomy, and the left cervical sympathetic ganglions were removed. In all but 3 similar injections of extract of the anterior lobe of the pituitary body produced definite exophthalmos in from twelve to twenty days. In some cases the exophthalmos was extreme and persisted after death. It was less marked on the side on which sympathectomy had been performed. The chief factors causing the exophthalmos were an increase of 100 per cent in the amount of retrobulbar fat and connective tissue, an increase of 40 per cent in the size of the dorsal lacrimal gland and an increase of 22 per cent in the volume of the extraocular muscles. An intracellular infiltration, presumably lipoid, found in the retrobulbar fat, connective tissue and muscle apparently was the predominant pathologic finding. Paulson [7] obtained exophthalmos in both thyroidectomized and nonthyroidectomized guinea pigs with daily injections of an extract containing the thyrotropic principle of the anterior lobe of the pituitary body (antuitrin T). Hypertrophy of the lacrimal glands was the predominant finding. This appeared as early as the tenth injection and was most marked after the eighteenth, becoming less with prolonged injections. Some degree of interstitial edema and degeneration was observed in the extraocular muscles of 4 guinea pigs, but these changes were not found consistently.

In a more recent study [8] in which he again used the extract containing the thyrotropic principle of the anterior lobe of the pituitary body, Paulson reported the production of exophthalmos, which was more marked in thyroidectomized guinea pigs than in similarly treated nonthyroidectomized animals. Degenerative changes in the extraocular muscles were found after only a few days of treatment. Similar, early degenerative changes were observed in both skeletal and cardiac muscles. Marked edema, which he felt was probably responsible for the exophthal-

6. Smelser, G. K.: Experimental Production of Exophthalmos Resembling That Found in Graves' Disease, Proc. Soc. Exper. Biol. & Med. **35**:128-130 (Oct.) 1936.

7. Paulson, D. L.: Experimental Exophthalmos in the Guinea Pig, Proc. Soc. Exper. Biol. & Med. **36**:604-605 (June) 1937.

8. Paulson, D. L.: Experimental Exophthalmos and Muscle Degeneration Induced by Thyrotropic Hormone, Proc. Staff Meet., Mayo Clin. **14**:828-832 (Dec. 27) 1939.

mos, was found in the extraocular muscles, retrobulbar fat and loose connective tissue. Both these changes and the exophthalmos were less evident in the animals given injections over prolonged periods. The changes in the muscles were considered to be atrophic and consisted of a separation of fibers, an increase in the nuclei of the sarcolemma and collection of lymphocytes.

From these studies it is not clear that the pathologic changes associated with the experimental production of exophthalmos are primarily those of myopathy, as has been found to be the case in the malignant exophthalmos of human beings. Furthermore, although the thyrotropic substance has been suspected of being the factor in the extracts of the anterior lobe of the pituitary body responsible for the production of exophthalmos, conclusive evidence has not been obtained to substantiate this impression. Experiments, therefore, were undertaken to clarify these points.

A series of five experiments were carried out on guinea pigs. Two preliminary experiments utilized alkaline extracts of the whole anterior lobe of the pituitary body [9] and thus corresponded to the studies reported by the majority of earlier workers. These experiments served to acquaint one with the problems and technics involved in this type of experimental work and confirmed the findings of earlier investigators, particularly those of Friedgood.[5] Daily injections were given for from five to seven months. An initial thyrotoxicosis was followed by a refractory period during which exophthalmos developed and slowly progressed in an irregular manner throughout the period of injection. Late in the experiments exophthalmos persisted even after the injections were discontinued, during narcosis and after death.

One of the chief difficulties encountered in this study concerned objective measurements of the exophthalmos. Direct methods proved impracticable in that they frightened the animals and resulted in struggling and sympathetic hyperactivity. Photographic methods required constant lighting conditions, which tended to make the animals close their eyes. The method that finally proved satisfactory utilized the principle of the camera lucida, which, without disturbance to the animals, permitted indirect tracings of the eyes to be made quickly and accurately from a superior angle (fig. 1). The outline of the orbit with respect to a line drawn between the tracings of the inner and the outer canthus formed the basis of the measurements (fig. 2). The canthi afford relatively fixed points with respect to the skull from which an accurate estimation of proptosis can be made. In this way faulty estimations involving variations in the retraction of the eyelids were avoided. Con-

9. The extracts used in these two experiments were supplied by Parke, Davis & Company and E. R. Squibb & Sons.

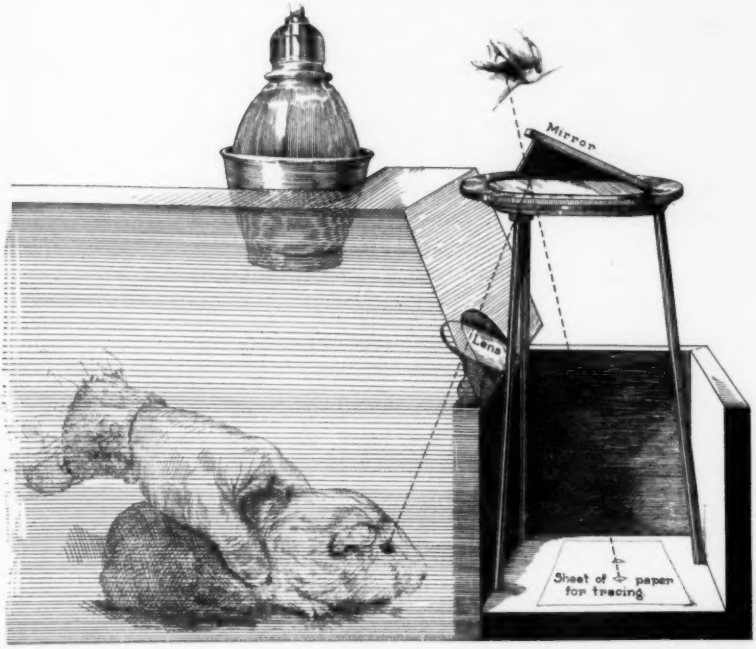

Fig. 1.—Optical apparatus which utilizes the principle of the camera lucida for tracing the images of the eyes of guinea pigs, indirectly and from a superior angle.

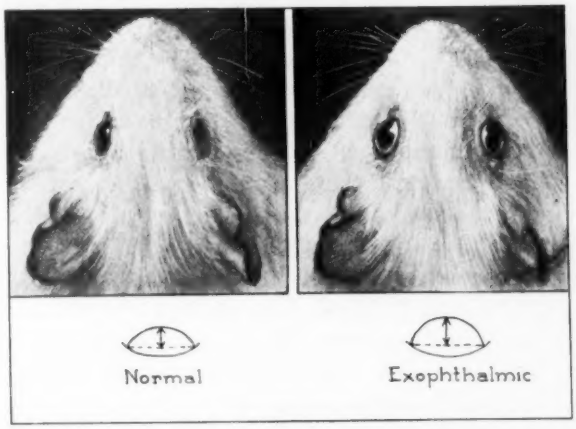

Fig. 2.—Normal and exophthalmic guinea pigs as seen from above and tracings of the images of the eyes of normal and exophthalmic guinea pigs as outlined through the optical apparatus used for measuring exophthalmos. The degree of proptosis represents the greatest distance between the outline of the cornea and a broken line joining the angles of the inner and outer canthi. The tracings are twice natural size.

trol studies showed this method to be accurate to within 0.5 mm. Thus, although the exophthalmos in these experiments measured only from 0.5 to 2 mm., the constancy of the measurements and the accuracy of the method made it certain that the phenomenon was real.

The extraocular muscles of these two groups proved of interest. Grossly, they were slightly larger in the group that received injections than in the controls. Microscopic study showed slight but definite degenerative changes and interstitial edema characterized by a loss of the cross striations, an increased number of small and deeply stained nuclei and a separation, breaking up and generally poor alinement of the muscle fibers. In addition, an infiltration of small round cells which tended to cluster or form "nests" was observed. Giant fibers were seen in the ocular muscles of the group given injections, and the staining was more irregular and unequal than in the extraocular muscles of the controls. Similar changes were not observed in the right deltoid muscle, selected as a control for other striated musculature.

The retrobulbar fat and tissues did not appear unusual in the group given injections. Occasional slight edematous changes were observed in both the retrobulbar tissues and the lacrimal glands, but these findings were not consistent and failed to show a correlation with the measured exophthalmos.

In a third experiment, guinea pigs were given daily injections for from four to five months with 80 units of a highly purified extract of the thyrotropic factor of the anterior lobe of the pituitary body, prepared according to the method described by Junkmann.[10] An initial acute thyrotoxicosis subsided into a refractory state, and with this, exophthalmos developed. It slowly progressed throughout the period of injection, and toward the end of the experiment the exophthalmos was so marked as to permit selection of the animals by casual observation. The proptosis varied from 1 to 2.5 mm. by measurement. The animals in this group showed greater changes than those in the two earlier experiments, and, correspondingly, the changes observed in the muscles of the eyes were more marked, especially the cellular infiltration and appearance of giant fibers.

It is of interest that in these three experiments the exophthalmos developed in the refractory period following the initial thyrotoxicosis. As exophthalmos has been reported after thyroidectomy [11] and the malignant form typically occurs in the presence of a low basal metabolic rate, thyroidectomy was performed in a fourth group of guinea pigs to check the possibility that simple hypothyroidism alone might be an

10. Drs. Uyei, Moon and Evans, of the department of experimental biology of the University of California, cooperated in the preparation of these extracts.

11. Gley, E.: De l'exophthalmie consécutive à la thyroidectomie; présentation d'animaux, Compt. rend. Soc. de biol. **68**:858-862, 1910.

etiologic factor in the production of exophthalmos. In four months of observation exophthalmos failed to develop in the animals in this group. Hypertrophy of the pituitary gland secondary to a hypothyroid state can thus be ruled out as a cause of exophthalmos.

In two of the three initial experiments in which the adrenal glands were studied, hypertrophy and hyperplasia of the adrenal cortex had been observed. In the experiment utilizing the Junkmann thyrotropic extract, the enlargement of the adrenal glands was grossly more than 50 per cent greater than that found in the control animals. Biologic assay of this preparation showed it to contain an adrenotropic substance up to 20 per cent by weight. It is conceivable that exophthalmos might be caused by either the adrenotropic hormone itself or the adrenocortical hormones elaborated as a result of the stimulatory effects of the adrenotropic hormone on the cortex of the adrenals. As the adrenocortical hormones are known to play a fundamental role in the reactivity of muscle and in metabolism,[12] the possibility of their producing a myopathy, such as occurs in malignant exophthalmos, required investigation. To test this possibility, a fifth experiment was performed in which a highly purified adrenotropic preparation [13] was used. Though a much higher dose of adrenotropic extract [10] was administered than was used in the preceding experiments, and though an enlargement of more than 50 per cent resulted in the adrenal glands, neither exophthalmos nor myopathy developed in these animals after three and one-half months of daily injections.

An analysis of the extracts used and the results obtained in these experiments likewise ruled out the gonadotropic, mammotropic and growth hormones of the anterior pituitary body as etiologic factors in the production of exophthalmos. The conclusion was thus reached that the extract containing the thyrotropic principle was responsible for the exophthalmos and the associated extraocular myopathy. Furthermore, the absence of other possible etiologic factors, such as were reported by Smelser [6] and Paulson [14] in their experiments of short duration, suggests that the myopathy observed in these experiments is of primary importance. The changes in the extraocular muscles of the experimental animals appeared similar to those found in human beings afflicted with malignant exophthalmos and correlated well with the degree of exophthalmos observed.

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12. (*a*) Ingle, D. J.: Work Capacity of the Adrenalectomized Rat Treated with Cortin, Am. J. Physiol. **116**:622-625 (Aug.) 1936. (*b*) Tipton, S. R.: The Effect of Cortin on the Electrolyte Changes in Cat Muscle During Stimulation and Recovery, ibid. **124**:322-327 (Nov.) 1938.

13. Moon, H. D.: Preparation and Biological Assay of Adrenocorticotropic Hormone, Proc. Soc. Exper. Biol. & Med. **35**:649-652 (Jan.) 1937.

14. Paulson (footnotes 7 and 8).

The evidence thus suggests that exophthalmos is related to the thyrotropic hormone of the anterior lobe of the pituitary body. The pathologic changes found in cases of exophthalmic goiter in human beings and the early changes found in experimental exophthalmos are edematous.[15] If proper endocrine adjustment fails to occur after thyroidectomy in human patients, the exophthalmos may continue to progress, and in the late malignant form a degenerative and fibrotic myopathy occurs which may be simulated in experimental exophthalmos by prolonged injections of thyrotropic extract.

SUMMARY AND CONCLUSIONS

The exophthalmos experimentally produced by injections of the extracts of the anterior lobe of the pituitary body was caused by the thyrotropic fraction. The exophthalmos developed in the refractory period following acute thyrotoxicosis produced by the action of the thyrotropic principle on the thyroid gland and progressed slowly in an irregular manner. After several months of injection, the exophthalmos was found to persist in spite of discontinuance of injections, narcosis or death.

Myopathy of the extraocular muscles was observed in the guinea pigs in which exophthalmos developed after injection of the extract. This change was sufficient to account for the degree of exophthalmos observed as well as its permanence following prolonged treatment. Other satisfactory explanations for the exophthalmos were not found. Qualitatively, the experimental myopathy was consistent with the changes found in the extraocular muscles of human patients afflicted with malignant exophthalmos.

ABSTRACT OF DISCUSSION

Dr. David Marine, New York: In any discussion of exophthalmos in exophthalmic goiter it is necessary to classify it into two types in order to give the general medical practitioner an idea of what is being talked about. The first type includes forms of exophthalmos without organic changes in the orbit and the second type forms with organic changes.

This paper deals mainly with the second type, that is, the type with anatomic changes. There are a small number of cases of the second type. Nearly all protrusions are of the first type. The second type has not been produced, at least I have not seen it, in the rabbit. It occurs only in the human beings and in the guinea pig and for the most part after subtotal thyroidectomy.

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15. (*a*) Moore, R. F.: A Note on the Exophthalmos and Limitations of the Eye Movements of Graves's Disease, Lancet **2**:701 (Oct. 2) 1920. (*b*) Burch, F. E.: The Exophthalmos of Graves Disease, Minnesota Med. **12**:668-675 (Nov.) 1929. (*c*) Paulson.[8]

Etiologically, the early stages (type 1) of exophthalmos are most important. The late stage is not so important in the study of the fundamental nature of the protrusion of the orbital contents. Unfortunately, one cannot carry over all the findings from the experimental animal to man, because there are differences that cannot yet be bridged, particularly of the so-called periorbital muscle; in man it is largely confined to the inferior orbital fissure, whereas in the lower animals it is relatively a huge cone-shaped muscle surrounding all the orbital contents except the lacrimal gland. In the lower animals it is easy to demonstrate that stimulation of that muscle will cause the orbital contents to protrude. That was done by Wagner in 1858, by MacCallum and Cornell in Baltimore, and recently in the Mayo Clinic, but in man this muscle is vestigial. One can reject the idea, then, that the periorbital muscle can cause the orbital contents to protrude in man as it can in the lower animals.

When one comes to the palpebral group of muscles, I think every one is agreed that spasm of the lid is due to increased tone of these smooth muscles; this is also true of the lower animals, so that the function of the muscles of the lid is similar in man and in lower animals. However, when one comes to the function of the periorbital muscle, one has to bridge a large gap. Still, I think there are some similarities even there.

As to the causation of exophthalmos, the medical profession has recently come to the view that it is in some way dependent on a polyglandular imbalance, and the old popular idea that it was due to oversecretion by the thyroid is not now considered seriously. It is hard to believe that the thyroid plays a positive role in this process when one can produce exophthalmos better after subtotal thyroidectomy and when administration of desiccated thyroid prevents and cures it. Dr. Aird has produced suggestive evidence that the thyrotropic factor of the pituitary is involved. Some years ago I made that same suggestion. I am less inclined to favor that suggestion today because of the fact that thyroidectomy favors the development of exophthalmos, and therefore one has to assume a polyglandular action of the thyrotropic factor. That is one objection. The other objection, of course, is that no one has succeeded in obtaining a pure thyrotropic factor—one free from other hormones of the anterior lobe of the pituitary body.

However, there is no question but that anterior pituitary extracts can produce typical exophthalmos in susceptible species.

Dr. Aird did not mention the gonads, but it is a fact that malignant exophthalmos is much more common in elderly men than in women. It is also striking that exophthalmos occurs much more frequently in the male rabbit than in the female. The sex hormone factor is important. Removal of the testes of rabbits caused an existing exophthalmos to regress. The administration of testosterone propionate, 10 mg. a day for four days, to these same rabbits reproduced the exophthalmos, and on discontinuance of it the exophthalmos again receded in a few days.

One other feature might be mentioned, that is, the muscular changes in exophthalmic goiter. As regards chemical changes in the muscles in this condition, Dr. Denis in 1916 examined a large series of patients with general diseases and found that the creatine content of the muscles was lower in cases of exophthalmic goiter than in cases of any other disease in which she made determinations. Today one would say the phosphocreatine content is greatly reduced in cases of exophthalmic

goiter. The smooth muscles, on the other hand, have normally a low phosphocreatine content, and it is unchanged. Smooth muscle tonicity and strength are unchanged, indeed often increased, in case of exophthalmic goiter.

The anatomic changes that Dr. Aird has described were first recognized probably by Askanazy in 1898. He spoke of the condition as a fatty degeneration, especially of the rectus abdominalis muscles, but it remained for Naffziger, of course, to give a complete description of it in the ocular muscles.

Why should the ocular muscles, those richly innervated, small muscles, show such extraordinary changes? I have always wondered if there was not some connection between the very rich motor innervation and the muscle fiber degeneration. It is obviously not due to the thyroid secretion.

Dr. Harry B. Friedgood, Boston: This problem is interesting from three points of view:

1. The first concerns the relation of experimental exophthalmos to the course of hyperthyroidism in guinea pigs given injections of chemically crude extracts of the anterior lobe of the pituitary body. The hyperthyroidism lasts about two to three weeks, and then the basal metabolic rate falls in spite of continued injections of the extract. Exophthalmos appears during the height of the hyperthyroidism, but it becomes more marked when the hyperthyroidism disappears and is most striking when the metabolism is abnormally low. During the early weeks of these daily injections, the exophthalmos fluctuates in prominence and may disappear if the injections are discontinued; but if the injections are continued for several months and then discontinued, the exophthalmos persists unabated. Early in the syndrome, therefore, the changes in the orbit are reversible; later, they are irreversible. One may conclude, therefore, first, that a decrease in function of the thyroid favors the development of exophthalmos as a result of injections of this extract and, secondly, that the changes in the orbit responsible for exophthalmos are reversible only for a limited time, after which they become irreversible.

Special importance may be attached to these conclusions, since the Naffziger syndrome is invariably associated with a low basal metabolic rate and because exophthalmos sometimes appears for the first time after thyroidectomy; or, in case it is already present, it becomes progressively more severe after operation.

2. What factor in the extract is responsible for the orbital changes which Dr. Aird has described? In some experiments done seven years ago, I found that as one continued the daily injections of extract over six months there were recurrent periods of hyperthyroidism at irregular intervals and that these recurrent exacerbations came soon after the administration of a new batch of extract was started. I knew that the protein content of these extracts varied moderately, and I could not relate the phenomenon to anything but the change in the batch of extract. During a discussion with Dr. P. E. Smith of the possible relation of these findings to the protein content of the extract, Dr. Smith suggested the desirability of studying the same problem with extracts which were deliberately prepared with known differences in protein content. Dr. Werner, in his laboratory, undertook this study and proved the point

in a well controlled series of experiments. One may conclude, therefore, that an antigen-antibody phenomenon is responsible for periodically interfering with the effectiveness of the thyrotropic hormone.

If one accepts this antigen-antibody theory, then one must assume that the thyrotropic extract becomes ineffective during the second, third or fourth week of its administration. However, the exophthalmos not only persists but becomes most marked when the thyrotropic principle has been inactivated by antibodies. In these circumstances, I must assume that it is not the thyrotropic principle itself which is producing exophthalmos. Since antibodies are apparently not formed against the agent responsible for exophthalmos, it is possible that the substance is not even of protein nature. The latter, in conjunction with a hypothyroid state, induces exophthalmos.

3. What preventive measures can one take against this serious orbital disorder? The startling similarity of the orbital pathologic process in these guinea pigs and in Naffziger's syndrome suggests a possibility, namely, the avoidance of a hypothyroid state. It is also important that the orbital changes may become irreversible, in which case nothing further can be done about the exophthalmos except through operation. In some work which I did six years ago it was shown that the administration of iodine to guinea pigs during their second week remission from pituitary hyperthyroidism caused the basal metabolic rate to fall to — 20 to 25 per cent. If a patient with exophthalmic goiter responds either to iodine or to thyroidectomy by a decrease to low minus levels of metabolism, one must suspect that he is a candidate for malignant exophthalmos. Thyroid substance should be administered to these patients early in the disease, because these changes are often irreversible.

I want to suggest a mechanism for the action of the thyroid in these cases. Hyperplasia of the thyroid occurs as a result of removal of part of the thyroid; compensatory atrophy of the thyroid takes place through the anterior pituitary gland as a result of the administration of thyroid substances. The administration of thyroid substance depresses the secretion of pituitary thyrotropic hormone, and it is possible that it thus also interferes with the secretion of the closely associated exophthalmos-producing substance.

The careful administration of thyroid substance in small doses should not be a harmful treatment for patients with exophthalmic goiter after iodine therapy and thyroidectomy when the basic metabolic rate drops below — 20 per cent.

Dr. Derrick Vail, Cincinnati: It is unnecessary to say how interested the ophthalmologist is in this experimental work so ably presented. The question of the paradoxic, or malignant, type of exophthalmos is indeed a grave one. Any evidence that one can obtain to point to the type of patient in whom this may develop, or to the type of therapy one can follow either to prevent or to treat it is of utmost importance.

I should like to show slides of 2 patients presenting this condition and point out the obvious appearance of pituitary dystrophy present prior to thyroidectomy.

This slide shows a man of 43, of Jewish extraction, obviously a pituitary type. Hyperthyroidism developed without exophthalmos, and the thyroid was removed. Four weeks later bilateral exophthalmos of the malignant type developed, such as is shown here.

Canthoplasty was attempted, but this was not successful, and eventually a Naffziger operation was performed on the right side.

This slide shows the loss of the eye so far as sight is concerned and development of an enormous leukoma of the cornea of the involved side.

The patient in this slide is a man of 36, also of Jewish extraction, who presented a picture suggestive of pituitary dysfunction. He did not have exophthalmos before the thyroid was removed, but following thyroidectomy exophthalmos developed in his right eye. This did not progress, fortunately, and canthoplasty helped him not only from a cosmetic but from a functional point of view.

I realize that these 2 cases do not constitute any great evidence in working out this problem, but they suggest, at least to me, that thyroidectomy should not be performed in a patient with pituitary dystrophy.

Dr. Robert B. Aird, San Francisco: I am especially fortunate in having Drs. Marine and Friedgood to discuss this subject. Following Schockaert's original work, Dr. Marine first suggested the thyrotropic hormone as the etiologic factor causing exophthalmos, and Dr. Friedgood first obtained an irreversible exophthalmos with prolonged injections of extracts of the anterior pituitary body. My work confirms theirs. The chief additional contribution of my studies consists in the demonstration of a myopathy as the cause of late and persistent experimental exophthalmos. A close parallel with Dr. Naffziger's clinical observations in patients with malignant exophthalmos is thus suggested.

As to the physiologic mechanism of exophthalmos, my experiments suggest that the thyrotropic hormone is an etiologic factor of fundamental importance and that the final, immediate cause in the late irreversible and malignant type of exophthalmos is a myopathy. The intermediate mechanism is not shown by my studies. Dr. Marine has suggested that the nerve supply to the extraocular muscles may in some way be involved. This occurred to me, but Bodian stains, which showed both the nerve endings and the end organs, failed to demonstrate changes which would support such a hypothesis.

Dr. Marine has raised the question of the causative hormone. Admittedly the use of impure extracts, which may cause both direct and indirect effects on a closely interrelated system of glands, is at best hazardous, and it was only after experiments with several different extracts and control studies on the pathologic changes produced in these glands by such extracts that I ventured to suggest the thyrotropic as the responsible hormone. As to the gonadotropic hormone, I believe the evidence is fairly conclusive in ruling it out as a factor.

The iodine test mentioned by Dr. Friedgood is extremely interesting. I have had no experience with it. In cases of early progressive exophthalmos I have considered the possible use of roentgen therapy to the hypophysis. If such therapy would affect the production of the thyrotropic hormone, its use would be logical and, if effective, would tend further to substantiate my ideas and the suggestive correlation between the exophthalmos of human beings and these experimental studies. Favorable results from such treatment could not be expected in cases of advanced exophthalmos in which fibrotic muscle changes have already occurred. Our experience with roentgen therapy, however, is still too limited to permit any opinion on this matter.

REPEATABILITY OF OPHTHALMOEIKONOMETER MEASUREMENTS

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One of the important steps in the study of aniseikonia has been the determination of the repeatability of the measurements of the difference in the sizes of the ocular images of patients by different clinicians by means of independent examinations on different ophthalmoeikonometers, not only at a given time but after the lapse of a period of time. In view of the fact that refractive data are also obtained with these measurements, the repeatability of the refractive settings would also be obtained. In so far as is known, similar studies of the repeatability of other ophthalmic measurements, e. g., refraction, have never been made. Opportunities for studies of this kind may be rare, because of the peculiar organization necessary and the cost involved, and the research clinic is fortunate in being able to carry through such a program, even though it is somewhat inconvenient and troublesome for the patients. This particular study is important from several points of view; first, from that of the reliability of the particular method of measurement; second, from that of the stability of the phenomenon being measured; third, from that of the reliability of different clinicians, and fourth, from that of the possible determination of other ocular factors which might influence the measurements.

REPEATABILITY OF MEASUREMENTS OF SIZE OF OCULAR IMAGES BY DIFFERENT CLINICIANS

Over a period of several months all patients who were examined for aniseikonia at the clinic were asked to undergo a second, or repeat, examination by another clinician on a second ophthalmoeikonometer.

The work is a collaboration of the foregoing members of the Research Committee in the Department of Research in Physiological Optics in the Dartmouth Eye Institute, of the Dartmouth Medical School.

The patients used in this study were, therefore, unselected except in so far as they had been referred for aniseikonic examination. Five clinicians, three of whom performed the greater part of the examinations, took part in the program. Instruments of the same design were used.

Procedure.—The procedure was as follows: The first clinician to see the patient made a regular examination. The refractive correction was determined, and with this correction the difference in the sizes of the ocular images was measured at the visual distances of 6 meters and 40 cm. On the completion of this examination the patient, with few exceptions, was immediately sent to a second clinician in another room who was informed of the refractive correction but not the difference in the sizes of the ocular images. He then proceeded to redetermine the refractive condition and the difference in the sizes of the ocular images. For this second examination the refractive correction found at the first examination was used.[1] Each clinician was advised to use the same technic, as far as possible, in making either the first or the second examination.

The differences found by the two clinicians in the measurements of the size of the ocular images in both the vertical and the horizontal meridian for distant as well as near vision were recorded by means of a special code, which permitted easy tabulation. The results of the two examinations were then compared.

The Instrumentation.—Since the type of eikonic target used in these tests for measuring the difference in the sizes of the ocular images was different from those previously reported in the literature,[2] a brief description of it is necessary. The principal unit of the instrument is, of course, the ophthalmoeikonometer, which remains unchanged;[3] only the type of eikonic target is new. In figure 1 the scheme is illustrated diagrammatically.

For near vision (40 cm.) a negative photographic plate was prepared from a pattern consisting of intersecting lines, a system of opposing arrows and a central ring. This plate was illuminated from behind. Pieces of polarizing film were placed over the arrows and numbers in such a way that the light passing through the even numbered arrows and letters was polarized in one plane, while that passing through the odd numbered arrows and letters was polarized in a plane at right angles to that of the even numbered ones. The ring and intersecting lines were not polarized. Polaroid plates were also mounted before each eye with the planes of polarization at right angles to each other but agreeing with those of the arrows. Thus, a patient looking into the instrument sees the ring and intersecting lines binocularly, the even numbered arrows with one eye and the odd numbered opposing arrows with the other eye. Fusion is maintained by the ring and lines, and, as has been indicated, these are sufficient, in general, to control the relative directions of the eyes when the subject is looking from the center of the target to any set of opposing arrows.[4]

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1. The procedure demanded that the refractive correction should not be altered in the second examination, for if it were the resultant difference in the sizes of the images might be changed and then the two tests would not be comparable.

2. Ames, A.; Gliddon, G. H., and Ogle, K. N.: Size and Shape of Ocular Images: I. Methods of Determination and Physiologic Significance, Arch. Ophth. **7**:576 (April) 1932.

3. For an illustration of the ophthalmoeikonometer see W. L. Hughes (Some Clinical Observations on Aniseikonia, Am. J. Ophth. **18**:715 [Aug.] 1935).

4. Burian, H.: Fusional Movements: The Role of Peripheral Retinal Stimuli, Arch. Ophth. **21**:486 (March) 1939.

If an observer has no difference in the relative sizes of the ocular images of the two eyes in the vertical and horizontal meridians and shows no fixation disparity,[5] he will see opposing arrows directly opposite each other; that is, corresponding opposing arrows will appear the same distance from the center of the target. If a fixation disparity does exist (and it usually does in the horizontal meridian), the arrows seen by one eye will appear displaced equally in the same direction as compared with the corresponding opposing arrows. If the relative sizes of the ocular images are unequal, then the arrows seen by the eye having the larger image will appear farther from the center of the target than the corresponding arrows seen by the other eye. Usually the displacements of the arrows due to fixation disparity do not prevent a comparison of the relative distances between corresponding arrows seen by the two eyes. Only in cases in which the displacement is large and unsteady will difficulty be encountered. By means of suitable zero verging power size lenses placed before one eye or the other, the sizes of the images can be equalized and thus the difference determined.

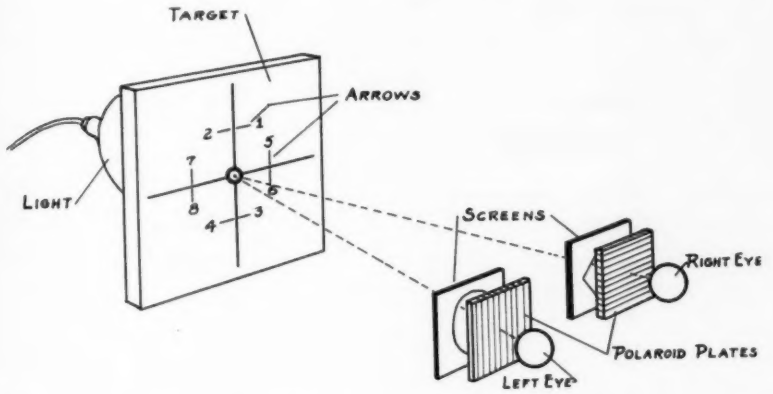

Fig. 1.—Schematic illustration of eikonic target used with the ophthalmoeikonometer.

For distant vision (6 meters) the same type of polarized pattern was projected from a lantern slide onto a screen which had been sprayed with aluminum paint.

Subjects.—In all, 102 patients participated in the study. The majority of these, 86, were regular patients referred to the clinic because of ocular symptoms which it was believed might be relieved if aniseikonia was diagnosed and corrected. Sixteen of the patients were persons in the community who, while not indicating any ocular discomfort, were sufficiently interested in the program to take part.

By the time the tests were completed it was evident that the results were going to be affected adversely by a number of the patients whose ocular condition was subnormal, so far as binocular vision was concerned, or with whom the method of their measurements would a priori prevent expectation of repeatability. There

5. Ames, A., Jr.; Ogle, K. N., and Gliddon, G. H.: Corresponding Retinal Points, the Horopter and Size and Shape of Ocular Images, J. Optic. Soc. America **22**:575 (Nov.) 1932.

were 27 patients who fell into this group,[6] this number, unfortunately, being a large proportion of the total number of patients. In view of this fact, the repeatability results were worked out for three groups: first, all of the 102 patients; second, the 75 "normal" persons, and third, the 27 persons comprising those for whom repeatability could not be expected. The last group will be designated the "special" group.

Figure 2 *A* shows a distribution diagram of the refractive errors of the whole group of patients according to the maximum refractive error in any meridian of either eye. The diagram is drawn so as to show the findings on both the "normal" and the "special" groups. It appears that the refractive errors of the "special" group differed little from those of the "normal" group, though perhaps the former showed more hypermetropia. The distribution of the group of patients used in

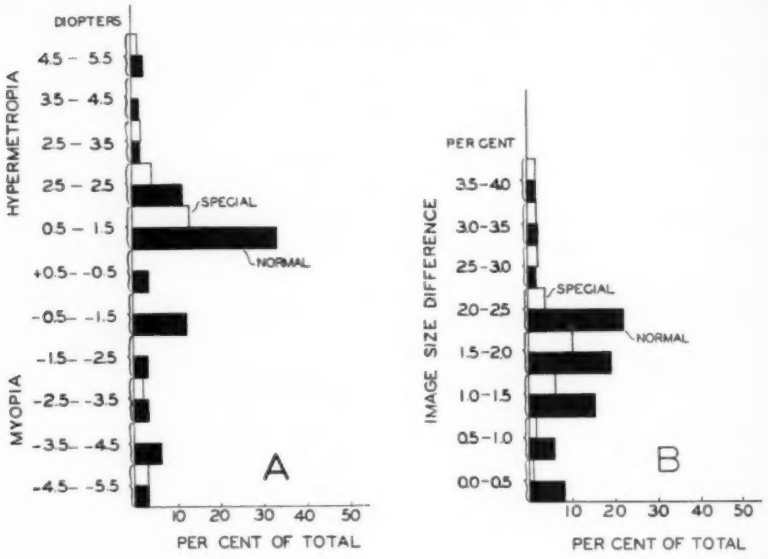

Fig. 2.—Histogram showing the distribution of the total 102 subjects given in the repeatability study according to: *A*, the maximum refractive error in any meridian of either eye and *B*, the maximum difference in the sizes of the ocular images measured in the vertical or horizontal meridians for distant vision.

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6. An analysis of this group showed: Two persons had alternating strabismus. Refractive corrections for 2 were very high, and small variations of the position of the head in the instrument would, therefore, cause variations in the measurable difference in the sizes of the ocular images. Eight persons included those who showed an unusual lack of sensitivity, poor discrimination, unsteadiness and lack of interest and who were otherwise unreliable subjects. For 12 subjects it was found that different technics had been used by the two clinicians. These included the use of prisms at one examination but not at the other, or changes in the refractive correction at the second examination, etc. Two of these subjects showed an unusual fatigue during the second examination which obviously prevented consistent results. Probably more subjects should have been included in this last category.

this study, in so far as the magnitude of the refractive error is concerned, was not very different from that usually found in the clinic.

Figure 2 *B* shows the distribution of the entire group of patients according to the maximum difference in the sizes of the ocular images measured in either the vertical or the horizontal meridian for distant vision. This distribution shows a maximum between 1.5 and 2 per cent, which is comparable to the average amount found in clinical cases of aniseikonia.[7] Hence, from the point of view of the measured difference in the sizes of the ocular images the whole group is an average group.

Analysis.—With this background for the repeatability comparisons in mind, the various tabulations of the results can be considered. The ideal aim of the study was to determine the repeatability of the ophthalmoeikonometer measurements without the influence of extraneous factors. It is impossible, of course, to eliminate fatigue or loss of sustained interest when such tests are prolonged, and these factors are important when reliance must be placed on subjective discriminations.

Observers with good eyes show a sensitivity to changes in the relative sizes of the ocular images of the order of 0.5 per cent or less;[8] hence, in comparison of the results of the two examinations 0.5 per cent was set as the lower limit within which better repeatability could not be expected. The best repeatability would be obtained when the measurements of the two tests check within 0.5 per cent difference in the sizes of the ocular images in both the vertical and the horizontal meridian for both distant and near vision. It has been evident in the clinic, however, that many patients show an unsteady ocular condition, with a resultant lowering of the sensitivity to difference size. Frequently, the result in a given examination can be obtained only by using a method of limits. Hence, the analysis of the data in this study also includes the repeatability within 0.75 and 1 per cent. In general, repeatability within 1 per cent would not be considered good, because the average difference in the sizes of the ocular images of patients having aniseikonia is around 1.75 to 2 per cent.

The first and most important tabulation in the analysis was the determination of the number of persons (percentage) whose repeatability in the two meridians for both distant and near vision was within 0.5, 0.75 and 1 per cent. The results for these categories are shown in column A of table 1. A study of this column shows that only 40 per cent of the subjects met the maximum requirement of checking within 0.5 per cent in both meridians at both visual distances. The measurements of over 50 per cent of the subjects checked within 0.75 per cent.

7. Carleton, E. H., and Madigan, L. F.: Size and Shape of Ocular Images: II. Clinical Significance, Arch. Ophth. **7**:720 (May) 1932.

8. Ames, A., Jr., and Ogle, K. N.: Size and Shape of Ocular Images: III. Visual Sensitivity to Differences in the Relative Sizes of the Ocular Images of the Two Eyes, Arch. Ophth. **7**:904 (June) 1932.

When the results for distant and near vision are considered separately, as shown in columns B and C of the same table, a decided improvement of the percentage occurs. For distant vision the measurements of 80 per cent of the patients repeat within 0.5 per cent and those for nearly 90 per cent repeat within 0.75 per cent in both meridians. The percentages for near vision are, however, less impressive. It is apparent from this study, as was already well known in the clinic, that the difficulties of measurement are much greater when made at near vision, especially in the horizontal meridian.

TABLE 1.—*Percentage of Patients Whose Measurements of Difference in the Sizes of the Ocular Images for the Two Tests Repeated Within Specified Limits of per Cent of Difference in Size When Grouped According to Combinations of Meridians and Visual Distances*

	No. in Group	Limits Within Which the Measurements Check		
		± 0.5%	± 0.75%	± 1%
A. Both meridians for distant and near vision				
Total	102	26	45	63
Retained	75	41	55	70
Discarded	27	0	11	41
B. Vertical and horizontal meridians for distant vision only				
Total	102	63	77	86
Retained	75	81	87	90
Discarded	27	30	48	70
C. Vertical and horizontal meridians for near vision only				
Total	102	32	49	64
Retained	75	46	63	73
Discarded	27	0	15	70
D. All meridians for distant and near vision excepting horizontal meridian for near vision				
Total	102	44	65	85
Retained	75	59	79	89
Discarded	27	11	30	63
E. Vertical meridian only—distant and near vision				
Total	102	50	71	87
Retained	75	64	84	93
Discarded	27	22	35	67

If the comparisons at near vision in the horizontal meridian are omitted (column D of table 1), a considerable improvement over columns A and C is evident. That the measurements in the vertical meridian are more reliable is also indicated by the tabulation in column E of the same table.

The essential repeatability results are found in table 1, but it was thought significant to consider separately the repeatability by meridians. This tabulation is shown in table 2. Here it is strikingly evident that, except for the horizontal meridian at near vision, the repeatability appears unusually high. The difference between these higher percentages and those of the previous table can, however, be understood; for a discrepancy in any one meridian or visual distance may nullify the apparent repeatability in any one case.

The problem concerning the discrepancies at near vision demands a separate study and cannot be discussed fully at this time. Experience has indicated, however, that the difficulty in the measurement at near vision in the horizontal meridian is usually encountered in persons who show a large and unsteady fixation disparity. The latter is usually, but not always, associated with high phorias, especially exophoria. The use of prisms often reduces the fixation disparity and thus assists in the measurement. In general, however, the use of prisms has been avoided as far as possible.

TABLE 2.—*Percentage of Patients Whose Measurements of Difference in the Sizes of the Ocular Images for the Two Tests Repeated Within Specified Limits of per Cent of Difference in Size When Grouped According to Single Meridians at a Given Visual Distance*

	No. in Group	Limits Within Which the Measurements Check			Correlation Coefficient	Probable Error of C. Coef.
		±0.5%	±0.75%	±1%		
Distant vision						
Vertical meridian						
Total	102	76	85	92		
Retained	75	90	93	95	0.87	0.02
Discarded	27	44	59	85		
Horizontal meridian						
Total	102	73	85	89		
Retained	75	86	90	93	0.76	0.03
Discarded	27	48	70	78		
Near vision						
Vertical meridian						
Total	102	59	77	90		
Retained	75	70	88	96	0.72	0.04
Discarded	27	33	52	74		
Horizontal meridian						
Total	102	45	54	66		
Retained	75	59	66	74	0.59	0.05
Discarded	27	10	30	48		

The conclusions from the analysis may be summarized as follows:

1. The repeatability of the measurements for distant vision in both the vertical and the horizontal meridian is very good, especially when compared with the results of most psychophysiologic measurements.

2. The measurements in the vertical meridian at near vision are fairly reliable.

3. With the type of eikonic target used in these experiments, no great reliance should be placed on the measurements obtained in the horizontal meridian at near vision if considered by themselves. However, in interpreting the results of an entire examination, they may be of some value.

In considering the foregoing conclusions, the following points should be kept in mind:

1. It is probable that in the second examination ocular fatigue was one of the important factors that tended to lower the accuracy of the

repeatability, especially since the average regular examination requires, at present, from one and one-half to two hours.

2. It was inevitable that the patient's attitude and cooperation would be different in the second examination than in the first, since the procedure was more familiar.

3. In spite of precaution and intentions to the contrary, clinicians do use slightly different technics in determining the differences in size, which might well influence the measurements when the method of limits is used, especially with patients having low sensitivity.

4. The general experience in the clinic is that many patients show an unsteady fixation disparity, especially at near vision, which results in a poorer discrimination of difference in the sizes of the ocular images. A number of the persons who fail to show a good repeatability of the test at near vision undoubtedly fall in this class.

Several tabulations were made to discover whether any particular ocular anomaly could be associated with the lack of repeatability. This included a correlation of the magnitudes of phoria, degree of refraction, ocular complaints and the magnitude of the difference in sizes measured. None of these factors, however, appears to influence the repeatability when considering the group as a whole, although they are undoubtedly important in interpreting the results in any given case.

REPEATABILITY OF MEASUREMENTS OF SIZE OF OCULAR IMAGES AFTER LAPSE OF A PERIOD OF TIME

In connection with the foregoing repeatability measurements, it is pertinent to ask how such measurements repeat over a longer period of time. Such a question is difficult to answer quantitatively because of the inherent clinical difficulty of obtaining a number of patients sufficiently great for a statistical treatment. While a considerable amount of data on subjects who have returned to the clinic for remeasurement have been obtained and are on file in the records, the work involved in analyzing all of these is not warranted at this time. In general, it can be stated that the measurements for each subject repeat rather well. Over long periods some differences are found, but these probably are no greater in proportion to corresponding refractive changes that might take place over the same period.

To illustrate the repeatability over a period of time, data on 10 subjects have been selected from the files, more or less at random, and the results have been tabulated as shown in table 3. Inspection of the table shows rather good repeatability. There are patients, of course, who have been examined over a period of several years whose measurements show variation. These results, in most of the cases, cannot be easily accounted for, though in many of them the variations can be attributed directly to the existent borderline squint.

TABLE 3.—*Data for Patients Whose Measurements on the Ophthalmoeikonometer Have Been Taken Over a Period of Time*

Patient	Date	Refraction	Difference in Size of Ocular Images
M. D. A.	11/30	R: +0.12 sph. ⊃ +0.37 cyl., ax. 90 L: +0.25 cyl., ax. 90	..... 1.25% o ⊃ 1.00%, ax. 90*
	6/38	R: +0.75 sph. L: +0.50 sph. ⊃ +0.50 cyl., ax. 90	..... 0.50% o ⊃ 1.25%, ax. 90
B.	7/35	R: +1.50 sph. ⊃ ⊂ −0.37 cyl., ax. 105 L: +2.00 sph. ⊃ ⊂ −0.62 cyl., ax. 90	1.50%, ax. 180 0.75%, ax. 90
	5/38	R: +1.75 sph. ⊃ ⊂ −0.50 cyl., ax. 105 L: +2.25 sph. ⊃ ⊂ −0.75 cyl., ax. 85	1.50%, ax. 180 0.75%, ax. 90
M. B.	6/33	R: +1.00 sph. ⊃ ⊂ +1.25 cyl., ax. 85 L: +2.50 sph. ⊃ ⊂ +0.75 cyl., ax. 170	2.00% o ⊃ 1.00%, ax. 175 .....
	10/35	R: +1.50 sph. ⊃ ⊂ +1.25 cyl., ax. 90 L: +2.75 sph. ⊃ ⊂ +0.75 cyl., ax. 170	1.00% o ⊃ 2.50%, ax. 180 .....
	6/37	R: +1.50 sph. ⊃ ⊂ +1.25 cyl., ax. 90 L: +3.00 sph. ⊃ ⊂ +0.75 cyl., ax. 180	1.25% o ⊃ 1.00%, ax. 180 .....
J. D'E.	9/33	R: Plano L: Plano	1.25% o ⊃ 2.00%, ax. 90 .....
	5/37	R: Plano L: Plano	1.00% o ⊃ 1.50%, ax. 90 .....
D. W. E.	11/32	R: −0.75 sph. ⊃ ⊂ −0.50 cyl., ax. 90 L: −0.50 sph. ⊃ ⊂ −0.50 cyl., ax. 80	..... 1.00%, ax. 180
	9/34	R: −0:50 sph. ⊃ ⊂ −1.25 cyl., ax. 90 L: −0:50 sph. ⊃ ⊂ −0.50 cyl., ax. 85	1.00%, ax. 90 .....
	1/38	R: +0.00 sph. ⊃ ⊂ −1.50 cyl., ax. 90 L: +0.25 sph. ⊃ ⊂ −1.00 cyl., ax. 85	1.25%, ax. 90 .....
W. F. H.	10/35	R: +2.25 sph. ⊃ ⊂ −0.50 cyl., ax. 75 L: +2.75 sph. ⊃ ⊂ −0.50 cyl., ax. 145	1.25% o .....
	10/39	R: +3.00 sph. ⊃ ⊂ −0.75 cyl., ax. 60 L: +3.50 sph. ⊃ ⊂ −0.75 cyl., ax. 175	0.75% o .....
J. H.	9/36	R: +0.75 sph. ⊃ ⊂ −1.50 cyl., ax. 5 L: −0.12 sph. ⊃ ⊂ −0.75 cyl., ax. 180	1.00%, ax. 180 1.75%, ax. 90
	9/39	R: +0.75 sph. ⊃ ⊂ −1.50 cyl., ax. 180 L: −0.25 sph. ⊃ ⊂ −0.75 cyl., ax. 180	1.25%, ax. 180 2.25%, ax. 90
C. E. L.	5/33	R: +1.37 sph. ⊃ ⊂ +0.25 cyl., ax. 180 L: +1.50 sph. ⊃ ⊂ +0.25 cyl., ax. 130	1.50% o .....
	5/35	R: +1.25 sph. L: +1.50 sph.	1.25% o 0.50%, ax. 120
	6/38	R: +1.62 sph. L: +1.62 sph.	0.75% o ⊃ 0.75%, ax. 90 .....
G. J. Mc.	8/30	R: +1.00 sph. ⊃ ⊂ +0.25 cyl., ax. 180 L: +0.75 sph. ⊃ ⊂ +0.50 cyl., ax. 90	0.25%, ax. 90 0.75%, ax. 180
	7/35	R: +1.00 sph. ⊃ ⊂ +0.25 cyl., ax. 180 L: +0.75 sph. ⊃ ⊂ +0.50 cyl., ax. 90	..... 1.50%, ax. 180
H. R. M.	8/30	R: +0.50 sph. ⊃ ⊂ +0.50 cyl., ax. 35 L: +0.62 sph. ⊃ ⊂ +0.25 cyl., ax. 70	..... 1.25% o
	9/37	R: +1.25 sph. L: +0.87 sph.	..... 1.25% o ⊃ 0.75%, ax. 90
	6/39	R: +1.25 sph. L: +0.75 sph.	..... 1.00% o
H. G. R.	12/29	R: +0.50 sph. ⊃ ⊂ −4.25 cyl., ax. 100 L: +1.00 sph. ⊃ ⊂ −4.00 cyl., ax. 75	1.50%, ax. 90 1.25%, ax. 30
	4/31	R: +0.37 sph. ⊃ ⊂ −4.25 cyl., ax. 100 L: +0.87 sph. ⊃ ⊂ −4.00 cyl., ax. 75	1.00%, ax. 90 1.75%, ax. 180
	10/34	R: +0.50 sph. ⊃ ⊂ −4.25 cyl., ax. 102 L: +1.00 sph. ⊃ ⊂ −4.00 cyl., ax. 72	1.50%, ax. 90 0.75%, ax. 180

* This reads: The left eye must be corrected with a 1.25 per cent overall size lens combined with a 1.00 per cent meridional size lens at axis 90 degrees.

REPEATABILITY OF THE REFRACTIVE SETTINGS

At the ocular examinations on the ophthalmoeikonometer, the refractive state of each eye is determined while the patient is using binocular vision by finding the conjugate point to the retina by means of reflected images of a point light source, the optical distances of which can be varied from the eye. The patient adjusts the position of this light point for the neatest and smallest size. This is a very sensitive method and is especially valuable for balancing the refractive corrections of the two eyes. The balancing points are usually determined by finding the maximum positive spherical correction that gives the best visual acuity.

In the repeatability tests for difference in the sizes of the ocular images, the conjugate points were also redetermined for each patient with the test lenses prescribed by the first clinician. A comparison between the two sets of data gives the accuracy with which this method of measuring refraction repeats. The pertinent data from a comparison of these tests are given in table 3.

TABLE 4.—*Tabulation of Important Facts Regarding the Reliability of the Refractive Technic When the Conjugate Points to the Retinas Are Determined with the Refraction of the Patient with Binocular Fixation*

	First Test	Second Test
(*a*) Mean distance of conjugate points with standard deviations..	+0.82 D.	+0.81 D.
Distant vision in diopters	0.25	0.25
(*b*) Probable error of single setting of refractive unit	0.06	0.06
(*c* Mean distance of conjugate points with standard deviations..	+2.51	+2.51
Near vision in diopters	0.26	0.27
(*d*) Probable error of single setting of refractive unit	0.09	0.09
(*e*) Per cent of cases in which differences between settings in the two tests were within +0.25 D.	Distance	90%
	Near	80%
(*f*) Per cent of cases in which the differences between the settings of the right eye and the left in both tests were within +0.25 D.	Distance	94%
	Near	90%

Since the dioptric distances of the tests were 0.16 diopter (distant vision of 6 meters) and 2.5 diopters (near vision of 40 cm.), the categories *a* and *c* in table 3 show how near the conjugate points to the retinas coincided with the true optical distance. By this method it is usually found that for distant vision the conjugate points lie from 0.5 to 1 diopter inside the true distance, though the visual acuity is not impaired. This phenomenon is probably due to the nature of the aberration bundle of light rays forming the image at the retina. In the examination the patient is asked to set the point light source as seen against a dark background at the optical distance at which the point of light appears smallest and neatest. The position of the waist of the aberration bundle, which is its smallest part, will vary somewhat with the contrast in the brightness of the light source to that of the background. The result is that when the intensity of the light is fairly strong, the eye is most sensitive to changes in the appearance of the image, though it makes

the eye appear more myopic compared with the results obtained with black letters on a white background. The clinician must, of course, be able to interpret the measurements in terms of the standard technics. The probable error of any one given setting is of the order of 0.1 diopter (categories *b* and *d* of table 4).

These results indicate that the repeatability and therefore the reliability of the refractive technic is very high.

SUMMARY

The analysis of the repeatability tests indicates definitely that the use of the ophthalmoeikonometer with the polarized eikonic targets is reliable for measuring differences in the sizes of the ocular images at distant vision. The tests in the horizontal meridian at near vision are less reliable, and considerable judgment is necessary to evaluate the findings obtained.

A random selection of subjects on whom remeasurements of differences in the sizes of the ocular images were made after the lapse of a period of several years showed a good repeatability and thus gave evidence for the stability of such differences.

The refractive technic employed on the ophthalmoeikonometer, in which binocular vision is maintained, is a reliable and accurate method of measuring and balancing the refraction of the two eyes.

This repeatability study has been of considerable value in the work of the institute, for in addition to providing the reliability of the measurement of differences in size it has suggested certain improvements and the direction of development of the present instrumentation and technic. The study has also focused attention to the need of repeatability data in other ophthalmic measurements.

Prof. A. Ames Jr. and Dr. Hermann M. Burian, offered many suggestions which materially aided in the carrying out of this project, and cooperation was given by the staff of the clinic, without which the project could not have been contemplated.

CIRSOID ANEURYSM OF THE ORBIT

REPORT OF TWO CASES

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Cirsoid aneurysms are not rare. Vascular changes about the orbit are reported under various titles: arteriovenous aneurysm, racemose aneurysm, pulsating angioma, cirsoid aneurysm and others. The cause in all cases is an abnormal communication between the arteries and the veins. The most commonly used title is cirsoid aneurysm.

Cirsoid aneurysms have been classified as tumors,[1] partial tumors[2] and arterial angiomas. Reid,[3] reporting numerous cases of cirsoid aneurysm, stated that the aneurysms are all the result of a free abnormal communication between the arteries and the veins and are in no sense neoplastic. They may be congenital or traumatic in origin.

Cirsoid aneurysms as a rule are widespread dilatations of neighboring arteries and veins. The size varies with the duration of the aneurysm. A continuous thrill and bruit are heard over the swelling, and the vessels involved pulsate. They differ from arterial angiomas, over which there is no thrill or bruit and usually no pulsation. The angioma contains arterial blood and is a common site of origin of cirsoid aneurysm.

The symptoms[4] complained of by the patient in cases of extraorbital cirsoid aneurysm vary with the duration, size and location of the lesions.

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2. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 250.

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4. Parsons, W. H., and Weston, W. G.: Traumatic Arteriovenous Aneurysm, South. M. J. **27**:703, 1934.

It is universally recognized that the heart is enlarged in established arteriovenous fistula. The cause of this enlargement is a controversial point. From experimental, clinical and anatomic evidence, the cardiac enlargement is explained by primary dilatation with a preponderance of the right ventricle, followed by hypertrophy, which later involves the whole heart. Branham's bradycardiac phenomenon is a marked slowing of the pulse on compression and obliteration of the communication. Cardiac enlargement has not been reported with orbital aneurysm.

Fig. 1 (case 1).—Preoperative appearance of patient. Note the swelling under the left ear, at the inner canthus of the right upper lid and in the conjunctiva of both eyes.

Two cases of cirsoid aneurysm of the orbit are presented: the first, a case of multiple congenital cirsoid aneurysms with orbital involvement, and the second, a cirsoid aneurysm of the orbit following trauma.

REPORT OF CASES

CASE 1.[5]—R. C., a white man aged 35, complained chiefly of severe headaches of diffuse distribution which had been present since childhood. Ten years ago he noticed a gradual increase in the prominence of the right eye with a small

5. This case was observed in consultation in the surgical service at the Cincinnati General Hospital and is presented with the permission of Drs. M. R. Reid and L. G. Herrmann.

lump in the upper lid. His visual acuity had not changed. Five years ago a pulsating lump appeared at the left angle of the jaw.

Except for measles and mumps in childhood, his general condition had been good. He offered the information that when he covered his ears he heard sounds in his head otherwise not heard. There was no history of orthopnea or edema of the extremities.

On physical examination the blood pressure in the right arm was 100 systolic and 70 diastolic and in the left arm 98 systolic and 65 diastolic.

Ocular examination revealed vision of 20/20 in each eye without correction. In the right upper lid above the inner canthus there was a fluctuant pulsating mass. A distinct murmur could be heard over the mass which diminished in intensity with pressure over the right common carotid artery. There were numerous

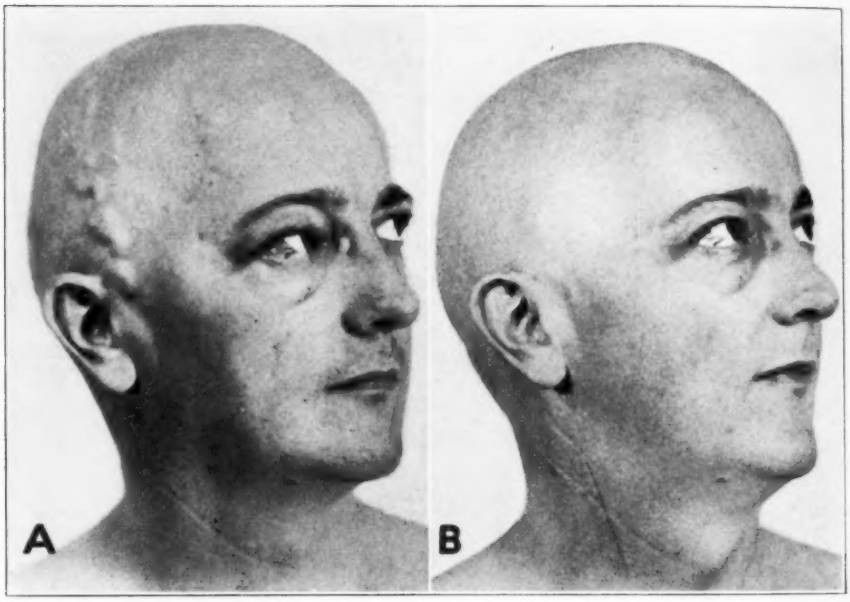

Fig. 2 (case 1).—*A*, preoperative appearance of patient. Note the swelling in the right upper lid, the dilated conjunctival veins and the dilated tortuous vessels of the scalp. Similar dilated vessels were present in the scalp on the left side. *B*, postoperative appearance of patient. The right external carotid and superior thyroid arteries have been ligated. The vessels of the scalp are no longer visible. The conjunctival vessels are smaller, and the mass in the right upper lid is less marked.

superficial dilated vessels in the bulbar conjunctiva, most marked on the temporal and nasal side of the cornea (figs. 1 and 2). In the left eye there were a few small tortuous vessels in the bulbar conjunctiva. The vessels of the fundi were slightly tortuous, did not pulsate and were not dilated. The field of vision for form and color was normal.

Posterior to the left angle of the jaw was a visible pulsatile mass the size of an olive. Pulsation was synchronous with the heart beat. Over it a to and fro thrill was felt and a definite murmur heard. Above the swelling, dilated pulsatile

channels could be followed over the occiput to the region of the lambda and the external occipital protuberance (fig. 2*A*). Similar channels were present on the right side running to the region of the lambda and the external occipital protuberance. Pressure over the carotid arteries diminished the murmurs over the aforementioned masses.

Neurologic examination gave negative results except for apparent weakness in the palate and total absence of the pharyngeal reflex. In the absence of other bulbar signs and a history of occasional regurgitation through the nose, the condition was interpreted as compression of the ninth cranial nerve in the jugular foramen by dilated vessels.

Fig. 3 (case 2).—Preoperative appearance of patient. The vessels in the left upper lid and the region of the inner canthus are not well seen. The swelling of the left upper lid can be seen and also the fulness of the nasopalpebral depression.

The remainder of the physical examination gave negative results. The Wassermann reaction of the blood was negative.

A diagnosis of multiple congenital cirsoid aneurysms was made.

Operation was done by Dr. L. G. Herrmann. The external carotid arteries and the superior thyroid arteries on each side were ligated at intervals of one week. The postoperative course was uneventful. On the patient's discharge from the hospital three weeks later there was no pulsation of the mass in the right lid; it had decreased in size, and the conjunctival vessels were markedly constricted (fig. 2*B*).

At a later examination this condition remained, but a pulsation was noted over the outer third of the left clavicle, and a to and fro bruit was heard over the pulsation. The patient felt well except for occasional headaches.

CASE 2.[6]—A white boy aged 8 years had injured his left eye eight months before the present examination by running a piece of chicken wire into the lower inner quadrant of the orbit. Four months later the left eyelids, particularly the upper lid, were noted to be swollen, and the conjunctival veins had become large and very red. Later the supraorbital vein became large, and varicosities appeared in the left eyelids and on the side of the nose around the inner canthus. The conjunctival veins were large and distended with arterial blood. They, as well as the large varicosities of the eyelids, nose and forehead, pulsated. There was no edema, which is usually marked when there is an intracranial arteriovenous fistula between the cavernous sinus and the internal carotid artery. The retinal veins were distended and pulsated. Vision was normal. On light palpation over the closed eye, a faint thrill could be felt. A bruit could be heard over the closed eye, nose and forehead. Temporary occlusion of the common carotid artery caused the eye to recede, the veins to collapse and the bruit to disappear. Because the aneurysm was most marked at the inner angle, it was thought that the abnormal communication was probably between branches of the external carotid artery and the neighboring veins.

A diagnosis was made of traumatic cirsoid aneurysm.

Operation was performed by Dr. M. R. Reid. At the time of operation it was found that ligation of the left external carotid artery had no effect on the aneurysm and that occlusion of the internal carotid completely stilled it; therefore, the common carotid artery was occluded by means of a removable aluminum band. The dilated veins in the lids were also excised.

Postoperatively there was slight weakness of the right arm and the right side of the face. This paralysis was probably due to cerebral anemia and disappeared in about two weeks. Had the symptoms demanded it, the metallic band on the common carotid artery could have been removed.

Ten years postoperatively there was no exophthalmos and no enlarged veins about the lids, nose or forehead. Vision was normal. The retinal vessels were of normal size and did not pulsate. No thrill or bruit was heard over or about the eye.

COMMENT

A brief outline of the vascular supply of the orbits and lids will emphasize the numerous veins and arteries to be encountered in this region, the widespread anastomosis between the branches and the proximity of the veins and arteries. In view of this vascularity, it is suprising that traumatic aneurysms are not more frequent. Dr. Derrick Vail,[7] in a discussion of his case in which the orbit was pierced by chicken wire, said that he was surprised that no reports had appeared of cirsoid aneurysm following retrobulbar injections in ophthalmic operations.

The arteries[8] supplying blood to the orbital contents are chiefly from the ophthalmic branch of the internal carotid artery and minor

6. This is a case of Dr. Derrick Vail and is reported with his permission. It was previously reported by M. R. Reid and J. McGuire (Am. J. Surg. **108**:643, 1938).

7. Vail, D.: Personal communication to the author.

8. Whitnall, S. E.: The Anatomy of the Human Orbit, ed. 2, New York, Oxford University Press, 1932.

additions from the infraorbital and middle meningeal branches of the internal maxillary artery. The branches of the ophthalmic artery are small but numerous and like the parent stem are characterized by a tortuosity, which obviates tension in ocular movements. Anastomoses are formed with extraorbital vessels, though not as freely as in the case of the ophthalmic veins. The orbital branches of the ophthalmic artery are: the lacrimal artery, which passes laterally in the orbit and ends in two palpebral vessels, which supply the conjunctiva and the skin of the lids; the muscular branches; the anterior and posterior ethmoid arteries, and the palpebral branches, which arise just below the trochlea,

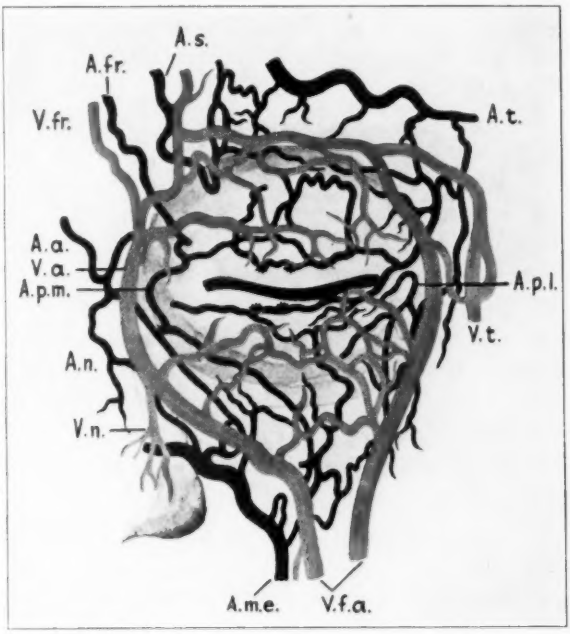

Fig. 4.—Arteries and veins of the left eyelids (after Merkel in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1897, vol. 1). *A.s.* indicates the supraorbital artery; *A.fr.*, the frontal artery; *V.fr.*, the frontal vein; *A.a.*, the angular artery; *V.a.*, the angular vein; *A.p.m.*, the medial palpebral artery; *A.n.*, the nasal artery; *V.n.*, the nasal vein; *A.m.e.*, the external maxillary artery; *V.f.a.*, the anterior facial vein; *V.t.*, the temporal vein; *A.t.*, the temporal artery; *A.p.l.*, the lateral palpebral artery, and **, the superior and inferior tarsal arches.

one going to each lid to form the superior and inferior tarsal arcades, which anastomose laterally with the palpebral branches of the lacrimal artery and also with the supraorbital and infraorbital arteries. The terminal branches are: the frontal artery, which leaves the orbit in the supratrochlear region, and the nasal artery, the real termination of

the ophthalmic artery, which leaves the orbit between the trochlea and the medial palpebral ligament and becomes continuous with the angular branch of the external maxillary artery.

The infraorbital artery is the terminal part of the internal maxillary artery, a branch of the external carotid artery. It originates in the pterygopalatine fossa, enters the orbit through the posterior end of the inferior orbital fissure and emerges on the face by the infraorbital foramen. It divides into palpebral, nasal and labial branches, which anastomose freely.

Whitnall's [9] description of the venous trunks in the orbit follows:

There are two main venous trunks. The superior ophthalmic vein is the chief one and is formed behind the medial corner of the upper eyelid by a union of the supraorbital angular veins of the face. It receives tributaries from the upper part of the eyeball (venae vorticosae and ciliary veins), from the upper medial ocular muscles and the two ethmoid veins. It also receives the lacrimal vein. The second main trunk is the inferior ophthalmic vein of the orbital floor. Its tributaries are from the lacrimal sac, the conjunctiva of the lower lid, the lower part of the eyeball and the lower and lateral ocular muscles. It anastomoses freely with the superior vein and in most cases empties into it at the apex of the orbit. The termination posteriorly of these trunks into the cavernous sinus is usually by a single channel, though separate entries of the superior vein and the central vein of the retina sometimes occur.

SUMMARY

Cirsoid aneurysm is an abnormal arteriovenous communication. It may be congenital or traumatic.

Cirsoid aneurysms pulsate. A thrill can be felt over them and a to and fro bruit heard.

A case of multiple congenital cirsoid aneurysms is presented which involves the lids and eyeball. Improvement was affected by ligation of the external carotid artery and the superior thyroid artery.

A case of traumatic cirsoid aneurysm of the orbit is reported in which complete healing was brought about by ligation of the external carotid artery, occlusion of the internal carotid with an aluminum band and local extirpation of some of the vessels in the lid.

A brief review of the vascular supply of the orbit and lids is presented.

Drs. Derrick Vail, M. R. Reid and L. G. Herrmann gave me permission to publish the details of these cases.

9. Whitnall, S. E., cited by Byers, W. G.: A Case of Encapsulated Angioma of the Orbit, Tr. Am. Ophth. Soc. **21**:144, 1923.

PRIMARY PITUITARY ADENOMA AND THE SYNDROME OF THE CAVERNOUS SINUS

A CLINICAL AND ANATOMIC STUDY

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PHILADELPHIA

Through the brilliant labors of Cushing, Frazier and de Schweinitz, the signs and symptoms establishing the diagnostic criteria for primary pituitary adenoma have become familiar to every student. Of the classic triad of signs, the chiasmal syndrome, constitutional dyspituitarism and roentgen evidence of hypophysial disease, the first mentioned has played the largest role in the recognition of pituitary adenoma. Indeed, the preeminence of the visual component in the semiology of pituitary adenoma led Henderson,[1] who recently published a critical review of Cushing's series of 338 cases, to declare: "It is exceptional for a chromophobe adenoma to be diagnosed or even suspected before it is sufficiently large to implicate the visual pathways. . . . . operation would hardly be justified before vision is affected." This remark may be taken as the general opinion expressed by the many who have written on the diagnosis of pituitary adenoma.

Though the nerves which supply the ocular muscles lie adjacent to the hypophysial fossa, their role in the symptoms of primary pituitary adenoma has been neglected. To be sure, one encounters in the literature passing allusions to cases in which palsy of the ocular nerves has been observed; usually it is said that this occurs either late or when the tumor has grown very large and has extended backward

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Read before the Section on Ophthalmology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Henderson, W. R.: The Pituitary Adenomata: A Follow-Up Study of the Surgical Results in Three Hundred and Thirty-Eight Cases, Brit. J. Surg. **36**:811, 1939.

into the interpeduncular space.[2] Cairns [3] recently wrote that palsy of the ocular nerves is uncommon in the life history of pituitary adenoma because the ocular nerves are protected from the lateral pressure of the expanding tumor by the carotid artery. Holloway [4] stated that while palsy of the ocular nerves may occur in the presence of pituitary adenoma, it is far more likely to occur with other types of tumor in the region of the sella turcica. Cairns,[3] Jefferson,[5] Frazier and Grant,[6] Holloway,[4] de Schweinitz and Carpenter,[7] Cushing,[8] Dott and Bailey,[9] Peet [10] and Dandy [11] have alluded to instances in their experience in which palsy of the ocular nerves apparently played a considerable role in the clinical picture of pituitary adenoma. They gave, however, no details of these cases. In some papers descriptions of paralysis of the ocular nerves are given but no special attention is drawn to it.

On the other hand, Uhthoff,[12] citing the interesting statistics from his experience, wrote that primary pituitary tumors associated with acromegaly showed an incidence of palsy of the third nerve in 11 per cent of cases, of paralysis of the sixth nerve in 2 per cent and of ophthal-

2. (*a*) Wohlwill, F.: Die pathologische Anatomie des Hirnbasis, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 6. (*b*) Posey, W. C., and Spiller, W. G.: The Eye and the Nervous System, Philadelphia, J. B. Lippincott Company, 1906. (*c*) Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1900, vol. 4, p. 604.

3. Cairns, H.: Peripheral Ocular Palsies from the Neurosurgical Point of View, Tr. Ophth. Soc. U. Kingdom (pt. 2) **58**:464, 1938.

4. Holloway, T. B.: Certain Pathologic Conditions About the Chiasm, Arch. Ophth. **6**:81 (July) 1931.

5. Jefferson, G.: On the Saccular Aneurysms of the Internal Carotid Artery, Brit. J. Surg. **26**:267, 1939.

6. Frazier, C. H., and Grant, F. C.: Pituitary Disorder: A Digest of One Hundred Cases with Remarks on the Surgical Treatment, J. A. M. A. **85**:1103 (Oct. 10) 1925.

7. de Schweinitz, G. E., and Carpenter, J. T.: The Ocular Symptoms of Lesions of the Optic Chiasm with the Report of Three Cases of Bitemporal Hemianopsia, J. A. M. A. **44**:81 (Jan. 14) 1905.

8. Cushing, H.: The Pituitary Body and Its Disorders, Philadelphia, J. B. Lippincott Company, 1912.

9. Dott, N. M.; Bailey, P., and Cushing, H.: A Consideration of the Hypophysial Adenomata, Brit. J. Surg. **13**:314, 1925.

10. Peet, M. M.: The Cranial Nerves, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1934, vol. 12, chap. 2, p. 15.

11. Dandy, W. E., in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1934, vol. 12, chap. 1, p. 607.

12. Uhthoff, W.: Ophthalmic Experiences and Considerations on the Surgery of Cerebral Tumors and Tower Skull, Being the Bowman Lecture, Tr. Ophth. Soc. U. Kingdom **34**:xvii-cxxiii, 1914.

moplegia in 1.5 per cent. But Davidoff,[13] in tabulating the findings in 100 cases of acromegaly, did not mention a single instance of paralysis of the ocular nerves. De Lapersonne and Cantonnet [14] stated that about 27 per cent of persons with hypophysial tumor but without acromegaly had palsy of the ocular nerves, but this statement is partly vitiated by the fact that they apparently included together several kinds of hypophysial and parahypophysial tumors. Velter,[15] agreeing with this figure, stated that 25 per cent of persons with pituitary adenoma in his experience presented palsy of the ocular nerves. Again he did not make a clear distinction between primary tumors of the hypophysis and other types of parahypophysial tumors. At any rate, it is difficult to reconcile these discrepant statistics.

Although a review of the literature clearly indicates that paralysis of the ocular nerves is by no means rare in cases of pituitary adenoma, there is nowhere an adequate discussion of its significance when associated with pituitary tumor, the mechanism of its production, the anatomic arrangement which permits it to occur, its diagnostic or prognostic importance or its surgical implications.

The occurrence of paralysis of the ocular nerves as an early, or in some cases the first, evidence of pituitary adenoma seems to have been first pointed out by Foix.[16] He referred to van Gehuchten as having been the first to observe this, but we have been unable to verify this in a perusal of van Gehuchten's posthumous book published by his son.[17] Foix described a case in which a pituitary tumor first evidenced itself by severe pain in the territory of the ophthalmic division of the fifth nerve and was associated with rapidly progressive unilateral paralysis of the third nerve, followed in turn by paralysis of the fourth and sixth nerves. Vision was unimpaired, and the visual fields were normal. He declared that this particular congeries of signs and symptoms was indicative of involvement of the structures in the external wall of the cavernous sinus. Although Jefferson [5] justifiably objected to Foix's being credited with priority and pointed out that

13. Davidoff, L. M.: Studies in Acromegaly: III. The Anamnesis and Symptomatology in One Hundred Cases, Endocrinology **10**:461, 1926.

14. de Lapersonne, F., and Cantonnet, A.: Troubles visuels produits par les tumeurs de l'hypophyse sans acromégalies, Arch. d'opht. **30**:65, 1910.

15. Velter, E.: Les troubles oculaires dans les syndromes hypophysaires, Rev. neurol. **38**:6 and 371, 1922.

16. Foix, C.: Syndrome de paroi externe des sinus caverneux (ophtalmoplégie unilatérale à marche rapidement progressive algie du territoire de l'ophtalmique). Amélioration considérable par le traitement radiothérapique, Rev. neurol. **38**:827, 1922.

17. van Gehuchten, A.: Les maladies nerveuses, edited by P. van Gehuchten, Louvain, A. Uystpruyst, 1920.

Bartholow [18] forty-eight years previously had defined the syndrome of the cavernous sinus in connection with a case of aneurysm, Foix [16] was apparently the first to describe the syndrome occurring with pituitary adenoma. While Foix only implied the generalization indirectly, de Lapersonne and Cantonnet [19] interpreted his remarks to mean that on the basis of the neuro-ophthalmologic involvement the clinical patterns of pituitary adenoma fell into two general groups: (1) the chiasmal syndrome with hemianopia, visual loss and atrophy of the optic nerve and (2) the syndrome of the external wall of the cavernous sinus, comprising involvement of the ocular nerves and the first division of the fifth nerve with preservation of the visual functions. It must be admitted that although Foix's patient was operated on by the transphenoidal route and that subsequently the patient's symptoms disappeared under high voltage roentgen treatment, no histologic report was given in the paper. The tumor, therefore, was presumably unverified.

Though this paper has been referred to by Rea,[20] Wohlwill,[2a] and de Lapersonne and Cantonnet,[19] we have been unable to find any one who has given serious attention to this conception. Cushing and Walker [21] in an early paper asserted that in 20 per cent of their cases of pituitary adenoma visual loss or visual field defects could not be demonstrated and that the diagnosis depended on the presence of other neighborhood signs. They did not, except in the most general way, define the precise grouping of signs on which the correct diagnoses were reached, nor did they elaborate their statement with illustrative cases. In Cushing's original monograph, however, he referred to cases of pituitary adenoma in which there was involvement of the ocular nerves as examples of adenomas showing prominent neighborhood signs (cases 6, 12, 16 and 20), but in none of these cases was the diagnosis histologically verified.

Recently Boschi and Campailla [22] published the report of a case under the title of "Syndrome of the Cavernous Sinus with Pituitary Adenoma" in which they stated that the combination of unilateral exophthalmos, edema of the eyelid and conjunctival hyperemia associated with pain in the trigeminal zone was indicative of involvement

18. Bartholow, R.: Aneurisms of the Arteries at the Base of the Brain: Their Symptomatology, Diagnosis and Treatment, Am. J. M. Sc. **64**:373, 1872.

19. de Lapersonne, F., and Cantonnet, A.: Manuel de neurologie oculaire, Paris, Masson & Cie, 1923.

20. Rea, R. L.: Neuro-Ophthalmology, St. Louis, C. V. Mosby Company, 1938.

21. Cushing, H., and Walker, C. B.: Distortions of the Visual Fields in Cases of Brain Tumor: Chiasmal Lesions with Especial Reference to Bitemporal Hemianopsia, Brain **37**:341, 1915.

22. Boschi, G., and Campailla, G.: Sindrome del seno cavernoso da adenoma ipofisario, Riv. oto-neuro-oftal. **9**:414, 1932.

of the cavernous sinus. Their patient in addition presented stigmas of dyspituitarism and roentgen evidence of destruction of the sella turcica. Improvement occurred under roentgen treatment, and the diagnosis therefore remains unverified.

A study of the 169 cases of verified pituitary adenoma in the collection of the Hospital of the University of Pennsylvania disclosed a group of significant size in which paralysis of the ocular nerves dominated the clinical picture and in a number of instances comprised the exclusive complaints and neurologic findings. This group, though showing variations in the clinical picture from case to case, presented in general a fairly consistent neurologic pattern and in the main conformed closely to the syndrome described by Foix.[16] The following cases are described to draw attention again to the implication by the pituitary adenoma of the ocular nerves and the other structures contained in the cavernous sinus. From a study of this material certain conclusions have been reached relative to the mechanism by which this syndrome is produced, the anatomic factors which allow it to occur, the establishment of features which permit differential diagnosis and the surgical implications. The group of cases is a selected one and by no means indicates the total incidence of palsy of the ocular nerves in the collection of cases of pituitary tumor, for in a number of cases not reported here palsy of these nerves was observed. We have confined our interest to those cases in which palsy of the ocular nerves and disturbances referable to the trigeminal nerve played an exclusive, predominant or large role in the symptoms of the pituitary adenoma.

REPORT OF CASES

Group 1.—This group consists of cases in which ocular paralysis of the ocular nerve and disturbances referable to the trigeminal nerve were the first as well as the exclusive complaints without impairment of visual function.

CASE 1.—The patient, a 39 year old woman, admitted to the hospital on Dec. 12, 1938, had been perfectly well so far as she knew until nine months before admission. At this time she suddenly experienced an intense pain in the left supraorbital region which lasted several hours and then passed away. Three months later severe pain again abruptly developed over the left eye and was followed in a few hours by complete ptosis of the left eyelid. Double vision was experienced when the lid was raised. Under iodide medication the ptosis partly disappeared but two months later again became complete. The patient then began to suffer from severe headaches, mainly over her left eye, but had no loss of vision. She had been amenorrheic since the age of 18 but stated that there had been no change in her sexual appetite. It was disclosed later that she had always been frigid.

Examination revealed an obese woman with thick skin and scanty hair. There was complete ptosis of the left eyelid associated with slight proptosis of the left eye. The third and fourth nerves were completely paralyzed, and the eye deviated

outward. The external rectus muscle functioned (fig. 1 *A*). The left pupil was dilated and fixed to light. Vision was 6/6 in both eyes. Both the visual fields and the optic disks were entirely normal. Roentgen examination of the skull revealed a markedly expanded and eroded sella turcica. Lateral views showed that the floor of the sella turcica was eroded asymmetrically, more on the left side (fig. 2 *a*). On the basis of the roentgen findings and the history of amenorrhea, operative exploration of the hypophysial region was decided on, although the precise diagnosis was in some doubt.

Left transfrontal craniotomy was performed (F. C. G.). When the region of the sella turcica was exposed, the carotid artery was visualized. Just lateral to this vessel there was seen the protruding tip of a purplish tumor. Aspiration yielded no blood; so the mass was incised. Reddish grumous material was curetted out and the capsule removed. The pituitary fossa was then exposed, and a large rounded tumor was seen between the limbs of the optic nerves over which the left optic nerve was slightly elevated. This was also incised and curetted out and as much as possible of the capsule removed. It was the opinion that the small

Fig. 1.—*A*, photograph taken at the time of operation, showing total paralysis of the third nerve. *B*, photograph taken ten months later, showing marked improvement, although the ptosis is still evident. The paralysis of internal rotation of the left globe is demonstrated during the attempt to look to the right.

lateral adenoma first encountered must have escaped laterally from the sella turcica, passed beneath the left optic nerve and over or around the internal carotid artery to appear in the middle fossa. This extension had evidently compressed the third and fourth nerves. The pathologic diagnosis was chromophobe adenoma.

After a stormy postoperative course, during which the bone flap was removed for excessive cerebral edema, the patient finally recovered and was discharged. Ten months later the palsy of the ocular nerves had diminished considerably (fig. 1 *B*), but vision had begun to fail. The patient was blind in the left eye and had a temporal hemianopia in the right eye.

Comment.—It is clear that in this case palsy of the ocular nerves was due to the lateral nodule which had compressed the structures in the cavernous sinus. This, combined with pain in the supraorbital region, pointed to involvement of three structures: the third and fourth

nerves and the first division of the fifth nerve. Although the corneal reflex was present, the acute, sharply localized pain suggested irritation of the first division of the fifth nerve. The abrupt onset may be explained perhaps by sudden rupture of the tumor into the cavernous sinus. The greater erosion of the hypophysial fossa on the left side is witness to the pathway the lateral extension followed.

CASE 2.—An 18 year old youth, admitted to the hospital on April 1, 1925, had been well until six months before admission. At that time a constant, intense boring pain developed in the right eye. A few days after the onset of the pain, his right eyelid dropped. He was seen by an ophthalmologist, who found com-

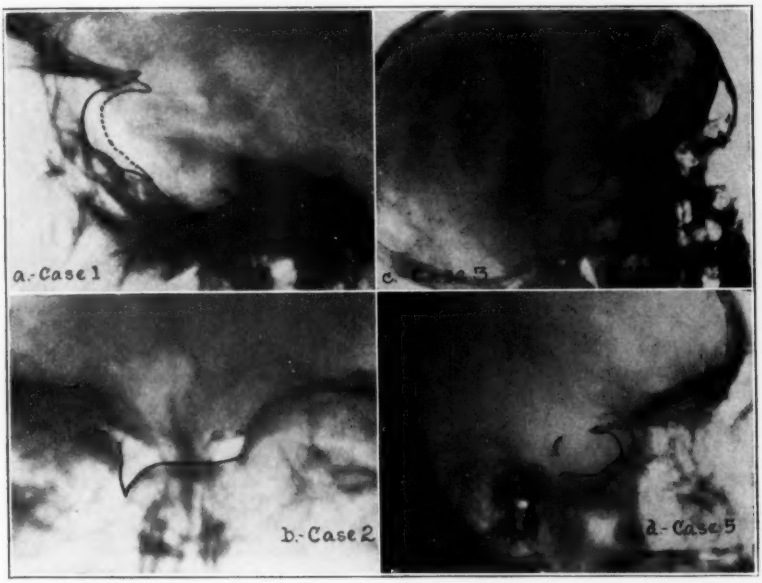

Fig. 2.—In *a* (case 1) the floor of the sella turcica is unequally eroded, the destruction being greater on the left (solid line). In *b* (case 2) there is an asymmetric erosion of the anterior portion of the sella turcica in the region of the sphenoid fissure which was accidentally, though fortunately, shown in the anteroposterior projection taken at an unusual angle. The erosion is on the right side, the side of the ocular palsies. In *c* (case 3) there is a slight but definite asymmetric erosion of the left side of the sella turcica (dotted line). In *d* (case 5) the anterior portion of the floor of the sella turcica and the left anterior clinoid process show considerably more destruction than does the right side. The left side is indicated by the dotted line.

plete palsy of the third nerve. His visual fields taken at that time were normal, and his visual acuity was normal. Four months later he began to suffer from headaches localized in the temples and vertex. Three months before admission he began to complain of some vague disturbances in vision.

Physical examination revealed a dull-looking fat boy whose complaint was headache. He showed a typical Fröhlich syndrome. There was complete paralysis of the right third nerve, with ptosis, a dilated fixed pupil and external deviation of the globe (fig. 3*A*). In addition, there was incomplete paralysis of the fourth nerve. The patient complained of numbness over the entire right side of the face, but disturbances of sensation could be found on objective testing only in the first division. Visual acuity was 6/9 uncorrected in both eyes. The visual fields were normal. The optic disks were normal.

Roentgen examination of the skull showed a markedly eroded and expanded sella turcica with encroachment on the sphenoid bone. In addition, lateral views showed an asymmetric erosion of the hypophysial fossa with the greatest destruction on the right side. An anteroposterior view fortunately showed considerable

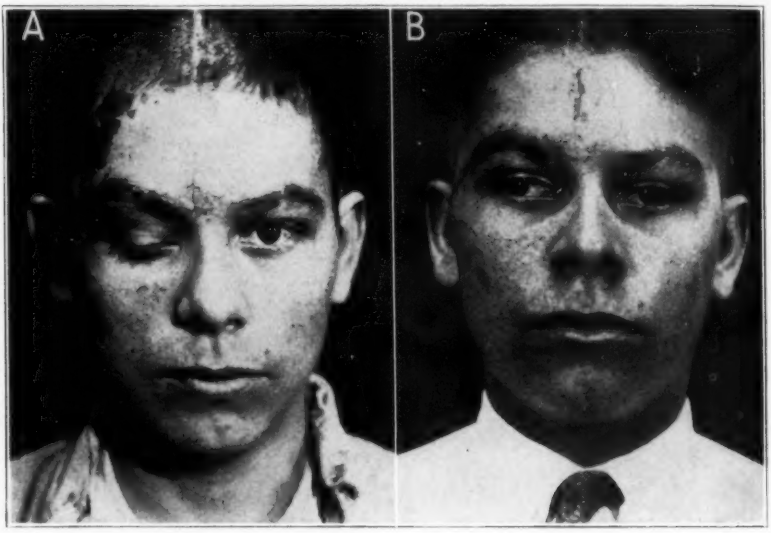

Fig. 3.—*A*, photograph taken at the time of operation, showing complete ptosis accompanying paralysis of the right third nerve. *B*, photograph taken four months later, showing marked but not complete return of function. The right eye deviates outward.

erosion of the anterior clinoid process and floor of the sella turcica on the right side (fig. 2*b*). In view of the constitutional evidences of dyspituitarism and the alterations in the contour of the hypophysial fossa, it was decided to explore the hypophysis.

Right transfrontal craniotomy was performed by Dr. Charles Frazier. His operative notes read in part: "When the right optic nerve was exposed two lesions were recognized, an adenoma of the pituitary and an accessory nodule protruding from the right side of the pituitary fossa and making its appearance between the outer side of the optic nerve and the internal carotid artery. The accessory nodule was removed and the main adenoma incised and evacuated." The pathologic diagnosis was chromophobe adenoma.

Three months later the palsy of the ocular nerves was clearing up (fig. 3 *B*). The patient lived six years after the operation. Vision failed completely toward the end of life.

Comment.—In this instance the third, fourth and fifth nerves were involved by the lateral extension of the tumor, which unquestionably had impinged on the cavernous sinus. The neurologic symptoms pointed only to involvement of these structures. The clue to the diagnosis was given by the evidences of endocrine disturbance and by the alterations in the contour of the sella turcica, which pointed to an intrasellar lesion. Objective evidences of visual involvement were lacking even at the time of the patient's admission to the hospital.

CASE 3.—A 47 year old man, admitted to the hospital on Oct. 29, 1929, had been well until five months before admission, when double vision abruptly developed. He was seen by his physician, who found only paralysis of the left external rectus muscle and internal strabismus. He was sent to an ophthalmologist, who reported that his visual acuity was 6/6 in both eyes. The visual fields were full, and the optic disks were normal. One month later a boring pain developed in the distribution of the second division of the left fifth nerve. This was punctuated by paroxysms of intense flashes of pain in the same region. In addition, he experienced sensations of tingling and of numbness in the left side of his face and tongue. There had been some difficulty in memory and of concentration and thinking. There had been no impairment in vision. There had been a rapid loss of libido.

Physical examination revealed a sick and somewhat apathetic man who was slow in his responses. There were ptosis of the left eyelid, paresis of the superior rectus muscle and paralysis of the external rectus muscle. Both pupils reacted to light. The left fifth nerve was anesthetic in all three divisions. The jaw deviated to the left. Visual acuity was 6/6 bilaterally. The fields were full, and the optic disks were of normal color. There was a questionable diminution in sensation of the right side of the palate. Roentgen examination of the skull showed marked destruction of the sella turcica with complete destruction of the floor, as well as asymmetric erosion (fig. 2 *C*). The left petrous apex was partly absorbed.

On the basis of the alterations of the hypophysial fossa, left transfrontal craniotomy was performed by Dr. Charles Frazier. The lesion was not exposed, as the patient collapsed while the cranioplastic flap was being reflected. He died nine days later, remaining in coma for the entire postoperative period.

Autopsy was performed. A large tumor was found arising from the pituitary fossa and extending in all directions. It had eroded the base of the anterior fossa and had perforated into the left orbit. A tongue of tumor had extended backward through the tentorial incisura into the posterior fossa. The lateral extension into the middle fossa had encroached on the left cavernous sinus, and the third and fourth nerves were embedded in the tumor mass. The tumor had encroached on and invaded the gasserian ganglion. The pathologic studies revealed an exceptionally cellular chromophobe adenoma. No mitoses were present however.

Comment.—The early symptoms of this patient were referable to involvement of the fifth and sixth cranial nerves. It is interesting that Foix remarked that the diagnosis of the syndrome of the cavernous

sinus is more definite when the symptoms begin with palsy of the sixth nerve and pain in the face. Eventually the third nerve was also implicated. Though autopsy disclosed a widely spreading tumor, there can be little doubt that the first point of extrusion was into the laterally lying cavernous sinus. Between the time of onset of the intial symptom and the time of operation, the highly cellular adenoma had overrun the boundaries of the sella turcica. It is especially interesting that even at this late period in the history of the tumor the optic chiasm was not clinically affected.

CASE 4.—A 50 year old man, admitted to the hospital on June 20, 1920, had been apparently well until eleven months before admission, at which time double vision suddenly developed. This was followed by severe and recurrent frontal headaches. From the time of onset of double vision he had noticed that his right eye slowly but steadily protruded. Six weeks before admission he experienced queer sensations on the right side of his face, as if it was being "lightly touched." For eight months there had been recurrent spells of giddiness and nausea. Libido had been absent for the year before admission.

Physical examination revealed a short obese man with the stigmas of dyspituitarism. There was paralysis of the right external rectus muscle with internal strabismus. Visual acuity was 6/6 in both eyes. The form fields were full, but there was a questionable contraction of the color fields and a questionable area of reduced vision temporal to the blindspot. Roentgen examination of the skull revealed marked destruction of the dorsum sellae and the posterior clinoid processes with enlargement of the pituitary fossa. The sphenoid sinus was encroached on.

On the basis of the roentgen findings transsphenoidal hypophysectomy was performed by Dr. Charles Frazier. When the vomer was removed a pulsating tumor was revealed filling up the sphenoid sinus. This was incised, and a yellow fluid gushed out.

After this procedure, most of the complaints disappeared. A few months later severe frontal headaches returned, and the patient experienced constant boring pains in the right side of the face associated with the sensation of numbness. He then started to lose vision, and the proptosis of his right eye reappeared. He was readmitted to the hospital, and on this occasion the right eye was found to be blind. Vision in the left eye was 5/25. There was a marked limitation of all movements of the right eye. Sensation was markedly impaired in all divisions of the right fifth nerve.

Right transfrontal craniotomy was performed by Dr. Charles Frazier, and a large tumor was encountered around the pituitary fossa. A profuse hemorrhage occurred from the cavernous sinus when an attempt was made to remove a portion of the tumor. The patient died a few hours after the termination of the operation.

Necropsy revealed the sella turcica filled with a soft tumor. This had extended laterally into the right middle fossa, where it had invaded and occupied the cavernous sinus and encroached on the gasserian ganglion. The third, fourth and sixth nerves were embedded in the tumor (fig. 4). The tumor was highly cellular and showed a few mitoses, so it was reported as a "chromophobe adenoma with malignant changes (?)." Unfortunately there are now no sections available.

Comment.—This is an especially interesting case, since it was possible to watch the progression of symptoms after the nature of the

tumor had been appreciated after the first operation. The initial symptom of palsy of the sixth nerve is distinctly unusual, since the sixth nerve is the most sheltered in position of all the ocular nerves in the cavernous sinus. The slight and questionable alterations in the visual fields were considered insignificant at the time of the patient's admission, and the decision to explore rested on the roentgen findings and the evidences of dyspituitarism. Aside from the paralysis of the sixth nerve, the occurrence of proptosis also pointed to involvement of the cavernous sinus. Unfortunately no note appears concerning the presence or absence of edema of the lids or retinal venous engorgement. Later the full-blown picture of implication of the structures in

Fig. 4 (case 4).—Drawing of the base of the skull as exposed at necropsy, clearly depicting the lateral escape of the adenoma into the middle fossa. The cavernous sinus is invaded and occupied by tumor. The remnant of the sixth nerve enters the tumor, but the other ocular nerves and the gasserian ganglion are embedded. Attention is called to the integrity of the optic chiasm and to the small nubbins of tumor which present in front of and behind the chiasm.

the cavernous sinus appeared with the development of paralysis of the third, fourth and fifth nerves. Visual loss was late in appearing. Autopsy adequately demonstrated the circumstances producing this unusual course of events. Particular attention should be paid to the artist's drawing of the tumor as it appeared at autopsy. It will be noted that the chiasm is undistorted and that the tumor appears to have grown both retrochiasmally and prechiasmally as well as laterally without growing vertically against the chiasm. This will be discussed later.

CASE 5.—A 40 year old woman, admitted to the hospital on Oct. 23, 1925, had been well until twenty-three months before admission. At this time she noted the onset of a persistent boring pain in the right orbit. Over the course of several weeks she noted that the right eye was protruding. This was particularly apparent when she strained at stool, and at this time the pain in her head became more intense. Ten months later hearing became decreased in the right ear, and the right side of her head felt numb when she combed her hair. She had several periods of hospitalization, but no diagnosis could be made. Attacks of diplopia and transient attacks of blurred vision made their appearance six or seven months after the onset of her troubles. The numbness in the right side of her face became worse, as did also the attacks of diplopia. She became deaf in the right ear. Her menses had been absent since the age of 28. There had been an

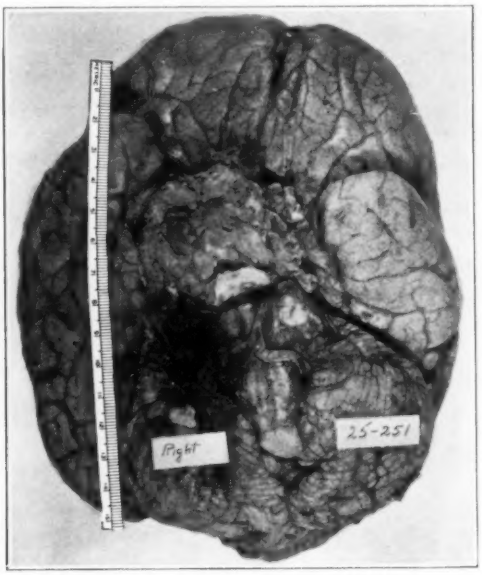

Fig. 5 (case 5).—Photograph of the autopsy specimen. It shows neither the optic chiasm nor the cavernous sinus, the latter being, of course, in the base of the skull. It does, however, show the predominant right-sided growth of the tumor into the middle fossa. It also demonstrates that pituitary tumors may grow very large without impairing vision. The extension into the posterior fossa and cerebellopontile angle can also be seen.

absence of libido for years. She had gained 60 pounds (27 Kg.) in the twelve years before admission.

Physical examination revealed a stout but fairly well proportioned woman. She was somewhat dull but cooperated well. Her gait was unsteady. There were paralysis of the right external rectus muscle and partial paralysis of the right third nerve, exhibited largely by paresis of the elevators of the eye. There was anesthesia of the entire right side of the face. The corneal reflex was absent. The right ear was deaf. Nystagmus was present in all directions of gaze. There was bilateral papilledema. Vision was 6/12 in the right eye and 6/9

in the left eye. The visual fields, however, were entirely normal. Roentgen examination of the skull showed marked destruction, though asymmetric, of the sella turcica and erosion of the right petrous apex (fig. 2*d*). The measurements of the pituitary fossa were 24 by 21 mm.

The diagnosis lay between a hypophysial tumor based on the roentgen findings or a tumor of the cerebellopontile angle based on the palsy of the cranial nerves. It was decided to explore the posterior fossa. The patient died twelve hours after exposure of the angle by Dr. Charles Frazier. Autopsy showed a large tumor springing from the pituitary fossa (fig. 5). As the illustration shows, the tumor grew laterally to one side of the midline. From the pituitary fossa it had spread anteriorly between the limbs of the optic nerves. By lateral extension the cavernous sinus and the gasserian ganglion had been completely surrounded. It filled the cavity of the ethmoid and sphenoid cells. A portion of the tumor had extended backward through the tentorium into the posterior fossa to occupy the right angle. The tip of the right petrosa was eroded, and just anterior to this point the ocular nerves were embedded in the tumor. The photograph of the brain unfortunately fails to show the salient and important features revealed by necropsy. The pathologic diagnosis was chromophobe adenoma.

Comment.—Although the tumor was very large, it had first evidenced itself by symptoms referable to the fifth, eighth and ocular nerves. No visual impairment had been complained of, and the fields were normal at the time of the patient's admission. The reduction of vision noted on testing was probably due to the papilledema and a certain amount of postpapillitic atrophy. In spite of the enormous mass of the tumor, the optic nerves showed little evidence of compression. The tumor had grown anteriorly and laterally and had missed the optic nerves. The tongue of tumor in the posterior fossa accounted for the false localizing signs. However, the invasion of the cavernous sinus seen at autopsy fully accounted for the clinical symptoms by pressure on the ocular and trigeminal nerves. The proptosis was also probably due to the obstruction of the cavernous sinus. The usual diagnostic reliance placed on the chiasmal syndrome had been misleading in its absence.

CASE 6.—A 41 year old woman, admitted to the hospital on April 20, 1930, had been well until five months before admission. At this time she began to have stabbing pains in both orbits and in both cheek bones. They came in attacks two or three times daily. These attacks of pain became more frequent and severe and prevented her from sleeping. Seven weeks before admission she awoke in the morning to find her left eye turned inward. After this, her eyes burned and smarted, but there was no loss in vision. There had been no alterations in weight or distribution of fat, and she had menstruated regularly.

Physical examination revealed a well built, cooperative and intelligent woman. There was paralysis of the left external rectus muscle. A diminished left corneal reflex was observed. Bilateral papilledema of 2 diopters was present. Vision in the right eye was 6/9 and in the left eye 6/30. The right visual field was entirely normal; the left showed a mild concentric contraction of the field to form and colors. Roentgen examination of the skull showed marked erosion and expansion

of the pituitary fossa. The left side of the fossa showed far greater erosion than the right (fig. 6*a*). The tip of the right petrosa was eroded. The basal metabolic rate was + 30.

Right transfrontal craniotomy was performed by Dr. Charles Frazier. His operative note reads in part: "Elevation of the frontal lobe revealed an enormous tumor. It spread anterior to the anterior clinoid processes, 2 to 3 cm. It appeared soft and friable. The left optic nerve was pushed far laterally so that it was out of sight. A large portion was removed." The pathologic diagnosis was chromophobe adenoma.

After operation the visual fields remained normal for more than a year. Visual impairment then gradually occurred. One year later the paralysis of the sixth nerve persisted and the eye could be brought only 15 degrees past the midline (fig. 7).

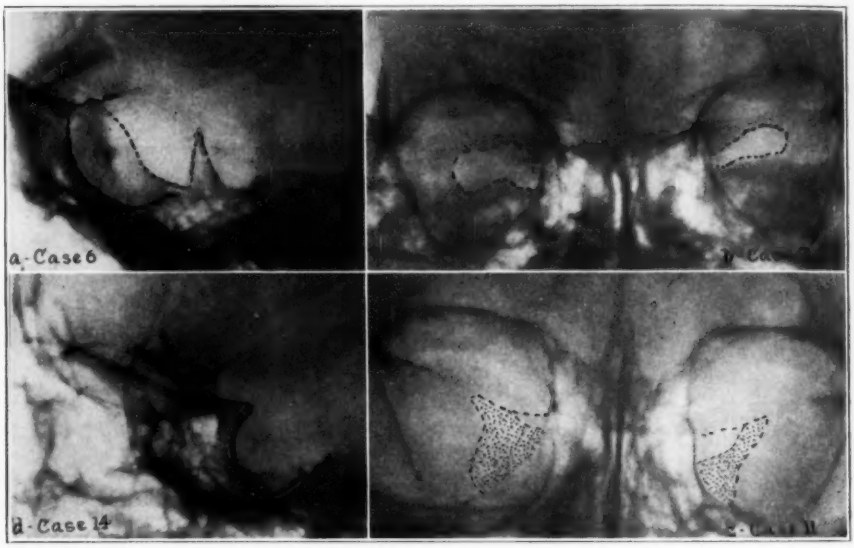

Fig. 6.—In *a* (case 6) there is marked destruction of the left side of the floor of the sella turcica. The destruction also involves the anterior portion of the body of the sphenoid bone where it forms the medial wall of the sphenoid fissure (solid line). The left anterior clinoid process is entirely absorbed. In *b* (case 7) both sphenoid fissures are enlarged in the anteroposterior projection, but the right one is considerably more affected. The density of the bone is the result of the acromegaly. In *c* (case 11) the anteroposterior film shows marked erosion and enlargement of the right sphenoid fissure. The medial wall of the fissure on the right side is absorbed and cannot be made out. In *d* (case 14) there is an irregular destruction of the floor of the sella turcica, the erosion being deepest on the right side (solid line). This could be easily determined with stereoscopic views.

Comment.—The large tumor in this case had not given rise to any visual complaint except diplopia. So far as the patient was aware the paralysis of the ocular nerve was her important complaint together with

pain in the orbits. Although palsy of the sixth nerve is commonly seen in the presence of increased intracranial pressure, we believe that the mechanism in this case was due to direct impingement on the nerve in the cavernous sinus. This conclusion is based on the associated hypalgesia in the first division of the fifth nerve, the fact that the paralysis did not disappear postoperatively and the fact that erosion of the tip of the petrosa clearly indicated the presence of the tumor at the point where the sixth nerve enters the cavernous sinus. The diagnosis of pituitary tumor was possible only on the basis of the roentgen findings, since evidences of dyspituitarism were lacking. The major neurologic signs can be assigned to involvement of the structures lying in the cavernous sinus.

In the previous 6 cases the symptoms were exclusively referred to the nerves lying in the cavernous sinus. The classic chiasmal syndrome

Fig. 7.—Photograph sent to us by the patient eighteen months after operation. Although it does not show the patient looking directly forward, the internal strabismus on the left is indicated by the unusual amount of sclera which can be seen and by the unusual degree of rotation of the left eye as the patient looks toward the right.

on which so much reliance is usually placed in the diagnosis of pituitary adenoma was conspicuous by its absence. The diagnoses were necessarily made on other grounds. Indeed in 1 case an incorrect operation was performed. This group corresponds in all the essential particulars to what Foix termed the syndrome of the external wall of the cavernous sinus.

Group 2.—In the second group of cases to be discussed the situation is only slightly different, though it must be admitted that so far as diagnosis is concerned, the difference is considerable. In this group implication of the structures of the cavernous sinus dominated the clinical picture, although examination disclosed evidences of variable degrees of injury to the optic nerves and chiasm.

This group consists of cases in which palsy of the ocular nerve and disturbances referable to the trigeminal nerve dominated the clinical picture but in which there was some evidence of injury to the optic chiasm.

CASE 7.—A 48 year old man, admitted to the hospital on Dec. 1, 1933, had been well until Nov. 19, 1933. On this date he was abruptly stricken with an agonizing pain in the head and headache, which persisted for forty-eight hours. At the end of this period his right eyelid suddenly dropped shut. After this incident his pain ceased. Until this experience he had been working steadily; there had been no visual complaints, and he stated on questioning that with glasses his vision had been good. He was transferred from another hospital on Dec. 1, 1933.

Physical examination disclosed a middle-aged man with acromegaloid features. At the time of examination he was drowsy and dull. There was total ophthalmoplegia of the right eye with ptosis and a dilated fixed pupil (fig. 8 *A*). When his fields were taken he was discovered to have bitemporal hemianopia. Vision in the right eye was 1/60 and in the left eye 6/60. There was no atrophy of the optic

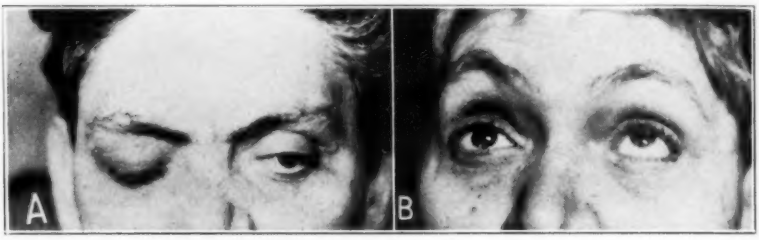

Fig. 8.—*A*, preoperative photograph showing complete paralysis of the third nerve and ptosis of the right eyelid. *B*, photograph taken six years later. The residual paralysis of the right third nerve is still demonstrable in the evident paresis of the right elevators on attempted upward gaze. A small degree of ptosis still remains.

nerve. Roentgen examination of the skull showed a large eroded, expanded sella turcica and encroachment on the sphenoid sinus. Both sphenoid fissures were eroded and indistinct, but the right was more involved than the left (fig. 6 *b*). There were obvious acromegalic changes in the bones of the skull.

Right transfrontal craniotomy was performed by Dr. Charles Frazier. His operative notes only state that an adenoma was found behind and beneath the chiasm. Unfortunately there are no details of the extension of the growth, so that an operative explanation of the ophthalmoplegia cannot be made. The right optic nerve was sectioned in order to remove a large part of the adenoma. The pathologic diagnosis was eosinophilic adenoma.

The vision improved in the left eye after operation. In 1939 vision in the left eye was 6/9. There was a superior temporal quadrantopia. There was still partial ptosis of the right eyelid and impairment in upward and downward rotations of the globe (fig. 8 *B*).

Comment.—Although the patient's complaint was ophthalmoplegia and he denied having previous visual difficulties, examination disclosed

marked loss of vision. It is possible that his vision deteriorated only after the onset of headache. Cairns mentioned the possibility that ophthalmoplegia and sudden loss of vision may occur abruptly when the tumor ruptures through the sellar diaphragm. This is suggested here by the fact that the optic nerve heads showed no evidence of atrophy on the patient's admission. There is little doubt, although it was not demonstrated at the operating table, that the cavernous sinus was encroached on by the tumor. The erosion and enlargement of the sphenoid fissures, particularly of the right one, testify to the lateral extension of the adenoma.

CASE 8.—A 50 year old man, admitted to the hospital on June 9, 1929, had been well until three and one-half months before admission. At this time double vision suddenly developed. By strong attempts at fusion he could overcome it for about fifteen minutes, after which his control broke. He noted some diminution in hearing about the same time. He did not complain of headache, but close questioning elicited the fact that there had been some impairment of vision for several months.

The patient was a well developed man, apparently in good health. The pupils were equal and active. The optic disks were normal. Visual acuity was 6/15 in the right eye and 6/22 in the left eye. The right field showed temporal hemianopia to red and contraction of the form field to the sixtieth isopter. The left field showed only temporal hemianopia to red, the form field being full. The left eye deviated outward owing to paresis of the internal rectus muscle. Roentgen examination of the skull showed an eroded and expanded sella turcica. The anterior posterior diameter was 15 mm., but the depth was uncertain.

Right transfrontal craniotomy was performed by Dr. Charles Frazier. The left optic nerve was found flattened over the surface of a cyst. This was largely removed. The pathologic diagnosis was chromophobe adenoma. After the operation the diplopia disappeared and vision improved. Ten years later, however, the right eye was blind, and vision in the left eye was reduced to reading headlines.

Comment.—The first complaint for which the patient sought medical advice was persistent diplopia. On examination this was found to be due to paralysis of the internal rectus muscle, innervated by the third nerve. Paralysis of an isolated muscle as a result of injury to the third nerve must be rare, but in this instance it was unequivocal. The evidences of injury to the optic chiasm and the enlargement of the hypophysial fossa made the diagnosis possible even in the absence of evidences of dyspituitarism.

CASE 9.—A 42 year old man, admitted to the hospital on Jan. 15, 1935, had been well until eleven months before admission to the hospital. At this time sharp shooting pains developed in the occiput. They were annoying but not severe. One month later his left eye suddenly turned inward. Diplopia was corrected by the use of a 22 degree prism and passed away in six weeks. He continued to have headache and occasional nausea. Eight and one-half months after the onset of his headache and seven months after the beginning of diplopia he began to notice blurring in the lateral fields of vision. Four weeks before admission he began to experience "waves of numbness" sweeping over the right side of his face.

These attacks would last but a minute or two. There had been a steady loss of sexual appetite in the year before admission and an accession of 10 pounds (4.5 Kg.) in weight.

The patient was a well developed and nourished man, clear, alert and cooperative. There was slight internal strabismus of the left eye. Vision in the right eye was 6/60 and in the left eye 6/22. There was a mild degree of bilateral atrophy of the optic nerve. There was no objective loss of sensation on the left side of his face. Examination of the visual field showed bitemporal hemianopia. Roentgen examination of the skull showed an extensive destruction of the sella turcica, erosion of both petrous apexes and erosion of both optic foramens.

Right transfrontal craniotomy was performed (F. C. G.). When the region of the sella turcica was exposed, the diaphragma sellae looked perfectly normal and flat. The left optic nerve appeared to be a little kinked as it entered the optic canal. A needle was inserted into the diaphragma sellae which seemed very tough. No fluid was obtained, but when the membrane was incised a large cavity was found below it. Some scrapings were obtained from the walls of this cavity. The pathologic diagnosis was chromophobe adenoma.

Comment.—This patient had symptoms referred to both the fifth and the sixth nerve. Although objective diminution of sensation could not be demonstrated, we think it certain that the fifth nerve was involved. It will be recalled that in 2 previous cases these sensations of numbness sweeping over the face antedated the development of frank anesthesia. The operative findings of a tough flat sellar diaphragm with no tumor above it but a large cavity below it makes it extremely difficult to account for the bitemporal hemianopia. The presence, however, of this stiff unyielding diaphragm with the large tumor cavity beneath it will be discussed later, as it has considerable bearing on the way some cases of the syndrome of the cavernous sinus are produced. The occurrence of diplopia and paresis of the ocular nerves eight and one-half months before the onset of visual disturbances is the important feature of this case.

CASE 10.—An 18 year old college student, admitted to the hospital on Sept. 25, 1923, had been well until eight weeks before admission, at which time diplopia suddenly developed. She was able to do her school work only by keeping one eye closed. On month later she began to notice some restriction in her lateral fields of vision. The degree of double vision also seemed to increase. For the three or four weeks prior to admission she experienced sharp transient pains in both orbits. She had been amenorrheic for three years before admission.

The patient was an obese young girl. The secondary sexual characters were poorly developed. There was paresis of the right external rectus muscle. Visual acuity was 6/6 in both eyes. The visual fields, however, showed a temporal paracentral scotoma in the right eye and temporal hemianopia in the left. Roentgen studies showed only a slightly enlarged sella turcica measuring 15 mm. anteroposteriorly and 11 mm. in depth. The basal metabolic rate was —20.

A probable diagnosis of pituitary adenoma was made, and the patient was given roentgen treatment, after which the diplopia disappeared and the visual fields returned to normal. Visual difficulties returned four years later, and at this time an exploration of the hypophysial fossa was carried out by Dr. Charles

Frazier and a cyst evacuated. The pathologic diagnosis was chromophobe adenoma. Over the course of the following thirteen years the patient had three more partial removals of the pituitary adenoma and at the time of writing she is still alive, though blind.

Comment.—In this instance the sixth nerve was apparently the only ocular nerve involved. This isolated involvement of the sixth nerve is unusual, the reasons for which will be discussed later. Although the diagnosis was possible because of the visual field defects, the diplopia was the first symptom and for a period of one month the only complaint. Direct involvement of the nerve must be assumed since there was an absence of intracranial hypertension.

Group 3.—In the third group of cases to be described the clinical pattern is different, although there are obvious and cleancut basic resemblances to the first two groups. In this group there were ample evidences of chiasmal injury, and the diagnosis of pituitary adenoma presented no great difficulties. There was, in addition, however, involvement of the structures contained in the cavernous sinus, so that an important part of the clinical symptoms was referred to these structures. In some cases these were still the predominant complaint of the patient though not necessarily the most important objective findings. In the cases in this group disturbances referable to the ocular and trigeminal nerves played an important role in the symptoms, but there were evidences of injury to the optic chiasm and optic nerves compatible with an intrasellar lesion.

CASE 11.—A 50 year old woman, admitted to the hospital on Nov. 11, 1930, began to experience headaches about thirty-four months before admission. Ten months after the onset of headaches double vision developed, which lasted for two months and then disappeared. The headaches became more severe and were punctuated with severe lancinating pains in the right orbit and just above the right eye. Nine months before admission the patient noted that vision was failing in the right eye and over the course of a few weeks that it was impaired in the left eye. Three weeks before admission the right eye turned inward. There had been a loss of weight of 20 pounds (9 Kg.) in the past two years. The menopause had occurred four years before admission.

The patient was a short and very obese woman. Her skin was thick, and her bodily hair was scanty. The right eye was entirely blind, and vision in her left eye was 6/9. Atrophy of the optic nerve was marked on the right and questionable on the left. There was temporal contraction of the left form field to the fiftieth isopter. There was partial ptosis of the right eyelid and impairment of upward movements of the right globe. The right pupil was dilated and fixed. The right external rectus muscle was paralyzed, and internal strabismus was apparent. Roentgen examination of the skull showed a widely destroyed sella turcica, which, however, was more eroded on the right side. The sphenoid fissure on the right side was markedly eroded and widened (fig. 6*c*). The basal metabolic rate was —8.

Left transfrontal craniotomy was performed by Dr. Charles Frazier. His operative notes read in part: "The left optic nerve was swollen to about twice

its usual size. What presented was not the capsule of the tumor but the sellar diaphragm, which was firm and resistant. A curet was introduced through this and seemed to break into a cyst. This freed the left optic nerve, since the domed but intact sellar diaphragm then collapsed. The interior of the sella was curetted out." The pathologic diagnosis was chromophobe adenoma.

The patient recovered vision in her left eye, and the field became normal. The paresis of the right third nerve still remained in part, as her postoperative photograph shows (fig. 9).

Comment.—Long before visual impairment was noted there had been an attack of diplopia, lasting two months. For most of the course of illness there had been sharp pains localized to the distribution of the first division of the right trigeminus nerve. Although obvious injury of the optic chiasm existed, there was in addition palsy of the third

Fig. 9.—Photograph taken ten days postoperatively, showing the residual ptosis of the right eyelid. Although a preoperative picture is not available, the hospital record states that the ptosis was marked.

and sixth nerves. The curious and interesting finding to which attention has been previously drawn was that the sellar diaphragm had not ruptured but had apparently been pushed up from below by the expanding tumor. This highly resistant membrane had forced the tumor to remain largely within the sella turcica, where it had eroded extensively and laterally as the findings indicated.

Case 12.—A 16 year old youth, admitted to the hospital on Dec. 19, 1935, had been well until eighteen months before admission. At this time he noted the beginning of a gradual loss of vision in both eyes. Three weeks before admission ptosis of the left eyelid suddenly developed. For three or four months before admission he had complained of shooting pain over both eyes.

Physical examination revealed a short, underdeveloped obese boy with a typical Fröhlich syndrome. Vision in the right eye was 2/60 and in the left eye 1/60.

There was right homonymous hemianopia. Both disks showed a moderate degree of atrophy of the optic nerve. There was incomplete ptosis of the left eyelid. The left pupil was larger than the right and reacted sluggishly to light. Roentgen examination of the skull revealed a slightly enlarged sella turcica measuring 14 mm. anteroposteriorly, and 9 mm. in depth.

Because of the difficulties in diagnosis, an encephalogram was made, which showed the absence of air in the chiasmic cistern. Left transfrontal craniotomy was performed (F. C. G.). When the chiasmal region was exposed, the left optic nerve was found pushed laterally by a bluish tumor, which projected outward between the optic nerve and the carotid artery. About 15 cc. of yellow fluid was obtained on aspiration. A large amount of beefy red tumor was removed with the cautery loop. The pathologic diagnosis was chromophobe adenoma.

The patient made an uneventful recovery, with temporary improvement in vision. Four years later the homonymous hemianopia was still present, and vision was reduced to 15/200 in the right eye and 5/200 in the left eye.

Comment.—Though there had been an obvious loss of vision, the dramatic onset of ptosis was the symptom which brought this patient into the hospital. The operative findings disclosed lateral extension of the tumor impinging on the cavernous sinus. Even with Fröhlich syndrome the occurrence of paralysis of the third nerve and a questionably enlarged sella turcica placed the diagnosis in doubt, and an encephalogram had to be made. The right homonymous hemianopia also indicated that the main mass of the tumor was behind and to the left of the chiasm.

Case 13.—A 40 year old woman, admitted to the hospital on May 4, 1924, complained of dimness of vision which began nineteen months before admission. This was noticed first in the lateral fields. Transsphenoidal hypophysectomy was performed at another clinic nine months after the onset of visual failure. After a short period of improvement, double vision developed. Two months after this occurred vision again began to fail. In a few months the right eye became blind and the left eye lost considerable vision. Six weeks before admission her right eyelid dropped shut. The patient had been amenorrheic since the age of 20.

Physical examination revealed a well developed and nourished woman who was mentally dull and slow in all her movements. Her features were large and coarse, and her skin was thick and cold. There was complete paralysis of the left third nerve, with ptosis, a dilated fixed pupil and external deviation of the globe. She was blind in the right eye, and vision in the left was 2/60. Roentgen examination of the skull showed destruction of the dorsum sellae and posterior clinoid processes with expansion of the sella turcica. The sphenoid sinus was almost obliterated.

Left transfrontal craniotomy was performed by Dr. Charles Frazier. A large cyst was found anterior to the chiasm. This was curetted out. The patient died of hyperthermia twenty-four hours postoperatively. Autopsy showed a large cystic tumor of the hypophysis which was tightly adherent to both carotid arteries. The pathologic diagnosis was chromophobe adenoma.

Comment.—The paralysis of the third nerve is explained by the autopsy revelation that the tumor had extended laterally to the carotid

arteries and had become adherent to them. Although this information is meager, when taken in conjunction with the clinical findings it is evident that the tumor encroached on the cavernous sinus. In this instance the paralysis of the third nerve raised no question of differential diagnosis, since the tumor had been verified at the first transsphenoidal operation.

CASE 14.—A 44 year old woman, admitted to the hospital on March 12, 1932, had noted for fourteen months a progressive restriction of her lateral fields of vision. Along with this, central visual acuity failed. Five months before admission double vision set in which varied in intensity from day to day. For three years preceding the onset of her visual symptoms she had suffered from recurrent attacks of sharp pain, starting in the right side of her nose and radiating into the right eye. There had been amenorrhea for sixteen years.

The patient was a short obese woman. There was paralysis of the right external rectus muscle with internal strabismus. Vision in the right eye was limited to perception of movement; in the left eye it was 6/9. There was temporal hemianopia in the left eye, but only a small island of vision remained in the right nasal field. Roentgen examination of the skull revealed erosion of the posterior clinoid processes and dorsum sellae and a ballooned fossa with definite asymmetric erosion and a double floor (fig. 6 *d*).

Right transfrontal craniotomy was performed by Dr. Charles Frazier, who found a large cyst over which the right optic nerve was stretched. No further anatomic details were given. The cyst was evacuated and curetted. The pathologic diagnosis was chromophobe adenoma.

The patient made a good recovery of vision in both eyes, but the diplopia persisted. This improved after a series of roentgen treatments.

Comment.—Although only the sixth nerve appears to have been involved, the attacks of pain sharply localized to the side of the nose and the right eye point to implication of the first division of the trigeminus nerve. This finding was noted in several other cases. Though her vision was failing, the patient was more annoyed by the diplopia. Throughout this series of cases double vision was a more disabling symptom than visual loss or field restriction and served as an urgent reason to bring the patients to the hospital.

SEMEIOLOGY OF PRIMARY PITUITARY TUMORS AND THE SYNDROME OF THE CAVERNOUS SINUS

While it is obvious that there are many differences between the foregoing cases, analysis of them shows a basic similarity which may be referred to involvement of the structures in the cavernous sinus.

Involvement of the Ocular Nerves.—The third nerve was the most commonly involved. This had been the experience of others who have observed paralysis of the ocular nerves in cases of pituitary tumor. There were 4 cases of total paralysis (1, 2, 7 and 13) and 6 cases of incomplete paralysis (3, 4, 5, 8, 11 and 12). In these cases of partial palsy of the third nerve the disturbance ranged from ptosis to paresis

of isolated movements. This appears to be somewhat unusual, since the accepted idea of paralysis of the third nerve is that peripheral lesions produce impairment of all functions of the nerve. For this we have no explanation except to assume that clinically, at least, this is not so and that early pressure against a nerve may impair at first only the functions mediated by the compressed fasciculus.

The opinion expressed by Jefferson [5] and by Cairns [3] that the internal carotid artery buffers the third nerve against pressure is certainly a generalization contradicted by these cases. It is questionable whether the infrequency of palsy of an ocular nerve can be explained entirely by this mechanism. Of this more will be said later.

In 2 cases the onset of paralysis of the third nerve was abrupt, which suggests the sudden impingement of the tumor on the nerve.

Involvement of the sixth nerve was present in 7 cases. In 3 of these cases (6, 10 and 14), it was the only ocular nerve paralyzed, although in cases 6 and 14 there was evidence of associated involvement of the fifth nerve. Other authors who have noticed the infrequent solitary implication of the sixth nerve have attributed it to the low-lying and sheltered position of the nerve in the cavernous sinus. However, the absolute as well as the relative positions of the ocular nerves in the cavernous sinus are subject to considerable variability, as may be easily seen by comparing the cross sectional illustrations of the cavernous sinus as they appear in the several textbooks of anatomy. The convolution of the carotid artery is also variable. In Spalteholz' [23] anatomic atlas the convolution of the carotid artery is pictured as lying forward in the sphenoid fissure, while in other anatomies it is depicted in various positions, sometimes occupying the posterior part of the carotid groove. In the more anteriorly placed convolutions, a laterally projecting nubbin of tumor could easily compress the sixth nerve. Sluder [24] also pointed out the fact that the sixth nerve may run superiorly in company with the fourth nerve.

In 4 cases (1, 2, 4 and 7) the fourth nerve was partly or completely paralyzed. In all instances, however, there was an accompanying involvement of some other ocular nerve.

Disturbances in the Trigeminal Field.—In 10 cases there was either pain, sensations of numbness or tingling, impaired sensation or decreased corneal reflex. These symptoms never occurred alone but always in association with palsy of the ocular nerves. Since the ophthalmic division occupies the most lateral position of the several nerves in the cavernous sinus, it is evident that other nerves would probably

23. Spalteholz, W.: Hand Atlas of Human Anatomy, translated by L. F. Barker, ed. 4, Philadelphia, J. B. Lippincott Company, 1923, vol. 3.

24. Sluder, G.: The Anatomy of the Sphenoid Fissure, Ann. Otol., Rhin. & Laryng. **32**:1108, 1923.

be affected if the tumor extended far enough laterally to implicate the fifth nerve. In cases 3 and 5, in which all three divisions of the fifth nerve were involved, there were accompanying multiple palsies of the ocular nerves. In only 2 cases (6 and 14) were the disturbances referable to the trigeminal nerve accompanied only by paralysis of the sixth nerve. In 5 cases (2, 3, 4, 5 and 6) there was either objective loss of sensation or impairment of the corneal reflex. In 3 cases (3, 4 and 5) all three divisions of the trigeminal nerve showed some evidence of involvement. In 6 cases there were sharply localized, acute shooting or boring pains in one division of the trigeminal field or subjective sensations of numbness. In all of the 6 cases in which there were only subjective sensations referable to the fifth nerve there was associated palsy of the ocular nerves, usually partial or complete paralysis of the third nerve.

The appearance of disturbances referable to the trigeminal nerve in cases of pituitary adenoma is probably more frequent than the literature indicates. Stewart [25] published the report of a case in which the initial symptom was pain in the upper division followed shortly by paralysis of the third nerve. Although the tumor was partly removed, it was necessary for Sir Victor Horsely to remove the gasserian ganglion some months later because of the persistent agonizing pain. Similar cases, though not as striking, in which there was clear evidence of involvement of one or more branches of the trigeminal nerve have been reported by Campailla,[26] Zöllner,[27] Bogen,[28] Habershon,[29] Verga [30] and Cushing.[8] The bitemporal headaches and orbital pains which are so commonly seen in cases of pituitary adenoma have been thought due to stretching of the dural envelope of the hypophysis which is supplied by the recurrent meningeal branches of the fifth nerve. It may be that the orbital pains at least are due to more direct pressure on the ophthalmic division lying lateral to the hypophysis and the pains thus referred to the terminations in the orbit.

Proptosis.—Proptosis was noted in 3 instances (1, 4 and 5). In these cases it was associated with multiple palsies of the ocular nerves and disturbances in the trigeminal field. Little information is available

25. Stewart, G.: Report of a Case of Pituitary Tumor, Proc. Roy. Soc. Med. (Sect. Neurol. & Ophth.) **6**:90, 1913.

26. Campailla, G.: Adenoma ipofisario ad estesa sindrome focale senza emianopsia, Riv. oto-neuro-oftal. **9**:461, 1932.

27. Zöllner, F.: Ein Fall von Tumor des Schädelbasis ausgehend von der Hypophyse, Arch. f. Psychiat. **44**:815, 1908.

28. Bogen, E. F.: Pituitary Tumor Causing Trifacial Neuralgia, J. Nerv. & Ment. Dis. **74**:722, 1931.

29. Habershon, cited by de Lapersonne and Cantonnet.[14]

30. Verga, G.: La patologic chirurgica dell'ipofosi, Pavia, Tipog. cooperativa, 1911, p. 185.

concerning the proptosis, but it was observed to recede in 2 cases after operation. The usual explanation given for proptosis associated with tumors of the cavernous sinus is venous engorgement as a result of compression of the cavernous sinus. If this is the true explanation one would think that the venous engorgement should be obvious on examination of the fundus or that evident edema of the eyelids should be present. No such observation was made in any of these cases although autopsy in 2 of them (4 and 5) showed complete neoplastic obliteration of the cavernous sinus. We are unable to explain this discrepancy.

Roentgen Findings.—In 11 cases either the original films or the positive photographs of the original films were available. In every case there were clear evidences of an intrasellar tumor, although in 2 cases (10 and 12) the enlargement of the sella turcica was minimal and the diagnosis of an intrasellar lesion was equivocal. In the other 4 cases, though the films are not available, it was the opinion of Dr. Henry Pancoast that they all showed alterations compatible with the diagnosis of pituitary adenoma. Unfortunately in the earlier years routine studies of the sphenoid fissures or optic canals were not made, and in some cases stereoscopic films were not taken, so that complete views are not available. In 8 cases, however, there was unequivocal roentgen evidence that the tumor had grown laterally. In 5 of these cases (1, 3, 5, 6 and 14) there was an obvious asymmetric erosion of the sella turcica with the formation of a double floor; the side of the greatest destruction corresponded to the side of the disturbances referable to ocular and trigeminal nerves. In 2 cases (7 and 11) evidence of unilateral extension was indicated by widening and erosion of the sphenoid fissure and in 1 case (2) by marked unilateral destruction of the anterior clinoid processes and the side of the hypophysial fossa, well demonstrated in an unusual and accidental anteroposterior projection. In addition to the alterations indicating a predominant unilateral erosion of the sella turcica, the other common findings in this series were expansion of the hypophysial fossa, destruction of the dorsum sellae and posterior clinoid processes, erosion of the sellar floor and encroachment of the tumor on the sphenoid sinuses. Erosion of the petrous apex was seen in 4 instances. This is a highly significant finding when present, for it definitely points to posterolateral extension of the tumor.

Endocrine Disturbances.—As would be expected in pituitary adenoma, the signs of dyspituitarism occurred in this series with the usual frequency, regardless of the unusual neighborhood signs. All but 2 cases (6 and 9) presented one or more unequivocal evidences of dyspituitarism. Acromegaly was present in case 7. The basis for the diagnosis of dysendocrinism in these cases was the familiar symptoms

and signs as amenorrhea, impotence and loss of libido, accession of weight, genital dystrophy, loss of hair, changes in the texture of the skin, drowsiness and loss of personality drive.

The high incidence of dyspituitarism is important in the differential diagnosis from other parahypophysial lesions, although, as will be indicated later, it is not an absolute differential phenomenon. This refers especially to tumors of the hypophysial duct. In the 2 cases in which endocrine disturbances were lacking, large tumors were found. Explanation of this fact is difficult, though for that matter it has always been difficult for clinicians to explain the absence of endocrine symptoms in pituitary adenoma. This has been so striking that all writers have classified their cases on the basis of the presence or absence of evidences of dyspituitarism.

Visual Disturbances.—These will not be considered in detail, since they are not germane to the subject of the paper and are covered amply in the case protocols. As a matter of fact, it is the absence or relative unimportance of the visual phenomena in at least groups 1 and 2 which makes these cases so unusual and serves to set them apart from the classic cases of pituitary adenoma.

ANATOMIC BASIS OF THE SYNDROME OF THE CAVERNOUS SINUS AND ANATOMIC STRUCTURE OF THE HYPOPHYSIAL REGION

The vagaries in the symptoms of pituitary adenoma depend in large part, as long recognized, on a number of anatomic divergences peculiar to different persons. On the other hand, unusual modes of growth play their part in determining the pattern and progression of symptoms. To a large extent, the anatomic structure of the sella turcica and, more particularly, the structure of the sphenoid bone influence the direction of growth of a tumor, so that the cause for the accessory nodules and the lateral extensions of the tumor lies in the anatomic peculiarities of this region.

The essential differences between the cases here described and the usual cases of pituitary adenoma is that the chiasm is affected little or not at all, and the involvement of the laterally lying structures dominates the clinical picture. While these two phenomena are closely related, they will, for the sake of clarity, be dealt with separately.

The reason that the chiasm is not affected, though not subject to direct proof in the cases here reported, doubtlessly depends on the anatomic variations in its position and in its relation to the sellar diaphragm. Schaeffer,[31] in his painstaking studies of this region, discovered that the space between the sellar diaphragm and the

31. Schaeffer, J. P.: Some Points in the Regional Anatomy of the Optic Pathways with Especial Reference to Tumors of the Hypophysis Cerebri and Resulting Ocular Changes, Anat. Rec. **28**:243, 1924.

under surface of the chiasm varied from a potential cleft to a vertical interval of 10 mm. He pointed out that in some instances more than a doubling in size of the hypophysis would be required before pressure on the chiasm could occur. This fact explains in part Cushing's and Walker's [21] statistics that 20 per cent of their patients did not show visual defects and probably also explains their declaration that the absence of any defect whatsoever in the visual fields did not speak against a primary intrasellar growth.

Another factor of great importance in determining the occurrence or the nature of the field defects in cases of pituitary adenoma, and which in some cases also explains their absence, is the wide variation in the relation of the optic chiasm to the sella turcica. The conventionalized conception of the chiasmal-sellar relations, as depicted in the anatomies, places the chiasm directly above the sella turcica. As a matter of fact, Schaeffer found that this occurred in but 12 per cent of the bodies examined, although in 79 per cent the chiasm lay wholly or partly above the sella turcica and the hypophysis. In 5 per cent of the bodies examined, the chiasm lay anterior to the sella turcica, and in 4 per cent it was located entirely behind. While in the vast majority of cases the location of the optic chiasm makes pressure on it inevitable in a vertically expanding tumor, it is possible, as Schaeffer pointed out, that in the posteriorly placed chiasms a hypophysial growth of considerable size could find its way anteriorly between the optic nerves. The same might well be true in the anteriorly placed chiasms, except that in this instance the tumor would grow posteriorly between the limbs of the optic tracts. Of interest in this connection is an exceptional case reported by Lloyd and Grant.[32] In their case a primary pituitary tumor of enormous size, measuring at autopsy 9 by 5 cm., had obliterated the third ventricle, extended back to fill the interpeduncular space, destroyed the left cerebral peduncle and the pons and extended into the posterior fossa. No visual field defects were found during life. Inspection of the photograph made post mortem shows how the tumor grew posteriorly between the limbs of the optic tracts, the chiasm being prefixed and far anterior.

Such anatomic variations may likely account for the absence of involvement of the optic chiasm or the only slight involvement in the first 9 cases. They do not explain, however, the reason that the tumors under consideration here tend to grow laterally to affect the structures in the cavernous sinuses.

Aside from the rapidity or sluggishness of growth, which varies from tumor to tumor and is presumably due to biochemical factors, it is well known that the direction of growth and the shape of tumors are determined in large part by the surrounding tissues and anatomic environ-

32. Lloyd, J. H., and Grant, F. C.: Tumor of the Hypophysis: Report of a Case, Arch. Neurol. & Psychiat. **12**:277 (Sept.) 1924.

ment. The structure of the sphenoid bone, the architecture of the sella turcica and the toughness of the sellar diaphragm are the most obvious factors that influence the mode of growth of pituitary adenomas.

In lightly pneumatized sphenoid bones, the sella turcica is deep and heavily constructed, with dense dorsum sellae and heavy, anterior and posterior clinoid processes. In these instances, as Schaeffer pointed out, a pituitary tumor would have difficulty escaping from the sella turcica, especially if the sellar diaphragm was tough, and would be forced to grow downward into the sphenoid sinus. On the other hand, in extensively pneumatized sphenoid bones, the sella turcica is shallow and possesses thin floors and fragile dorsum sellae. In these instances an adenoma would have relatively little difficulty, especially if the sellar diaphragm were weak, in escaping the confines of the sella turcica. The wide variability of the structure of the sphenoid bone and the development of the sphenoid sinuses have been described in the excellent monographs by Onodi [33] and Canuyt and Terracol [34] and in the papers of Cope [35] and Sluder.[36]

The density of the sellar diaphragm as just mentioned plays a considerable role, at least in certain instances, in determining the ability of the pituitary adenoma to expand out of the sella turcica. Again we refer to the fundamental observations of Schaeffer, who studied the structure of the sellar diaphragm. He found that it varied from a dense, strong membrane with only a small perforation for the penetration of the infundibulum to a mere peripheral rim with a relatively huge infundibular foramen. It appeared entirely reasonable to him that the structure of the diaphragm should influence the growth of a hypophysial tumor.

That this assumption is more than speculation is clearly indicated by the operative findings in cases 9 and 11. In both of these a thick, tough, unruptured sellar diaphragm was found, underneath which there was a large eroded cavity containing the cystic adenoma. Heuer, on the other hand, expressed the belief that the resistance of the sellar diaphragm is inconsequential and that the adenoma bursts through it early and easily. This may be generally true but obviously is not a rule. In the type of case in which the diaphragm does not rupture the adenoma can extend only laterally.

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33. Onodi, A.: The Optic Nerve and the Accessory Sinuses of the Nose, translated by J. Luckhoff, New York, William Wood & Company, 1910.

34. Canuyt, G., and Terracol, J.: Le sinus sphénoïdal, Paris, Masson & Cie, 1925.

35. Cope, V. Z.: The Internal Structure of the Sphenoidal Sinus, J. Anat. **51**:127, 1927.

36. Sluder, G.: The Anatomic and Clinical Relations of the Sphenoid Sinus to the Cavernous Sinus and the Third, Fourth, Fifth, Sixth and Vidian Nerves, Ann. Otol., Rhin. & Laryng. **22**:725, 1913.

The data already referred to deal with the factors which determine the direction and mode of growth of a pituitary adenoma. Though direct proof is lacking concerning the antemortem anatomic structure of the sphenoid bone, the sella turcica and the sellar diaphragm, except in the 2 cases mentioned, it is justifiable to assume that a combination of anatomic factors forced the tumors to grow down and laterally. Indirect evidence that some such combination existed may be inferred from the observations at the autopsy table in cases 3, 4, 5 and 13 in which lateral extensions were found; in cases 1, 2 and 12 in which lateral nodules were found at the operating table, and cases 6, 7, 11 and 14 in which there were clear roentgenographic evidences of lateral extension.

It seems a self-evident fact that the syndrome of the cavernous sinus requires that the pituitary adenoma grow laterally. Heuer,[37] who studied the direction of growth of these tumors, remarked that while the great majority of them grew anteriorly, a certain number primarily grew laterally. He did not, however, explain this observation on anatomic grounds. A warranted assumption would be that the line of least resistance influences the direction of growth. Inspection of the anatomic structure of this region shows that a tumor obeying this principle may easily grow laterally. The usual textbooks of anatomy offer little detailed information concerning the structure of the walls of the cavernous sinus and the relation of the hypophysis to the cavernous sinus.

The hypophysial fossa, though formed by a depression in the sphenoid bone and bounded anteriorly and posteriorly by bony walls, has no lateral walls of bone, so that the hypophysis which rests in it is closed in by the cavernous sinuses on either side. The standard anatomies do not emphasize this point, and their conventional illustrations of this region, usually shown in views of the base of the skull, are somewhat misleading. Fisher [38] and Cushing at least have made passing mention of this fact. On the other hand, the usual coronal sections depicted are almost routinely artists' conceptions and not drawings of actual specimens. Prof. Oscar V. Batson [39] informs us that studies of serial coronal sections through this region are lacking in the anatomic literature. An illustration in Corning's textbook,[40] however, is an excellent one and shows these relations clearly in a drawing of a coronal section passing

37. Heuer, G. J.: Surgical Experiences with an Intracranial Approach to Chiasmal Lesions, Arch. Surg. **1**:368 (Sept.) 1920.

38. Fisher, J. H., in discussion on Schäfer, E. H.: The Structure and Functions of the Pituitary Body, Proc. Roy. Soc. Med. (Sect. Neurol. & Ophth.) **6**:67, 1913.

39. Batson, O. V.: Personal communication to the authors.

40. Corning, H. K.: Lehrbuch der topographischen Anatomie für Studierende und Aerzte, Wiesbaden, J. F. Bergmann, 1907, p. 24.

through the center of the pituitary body (fig. 10). A similar though less detailed drawing may be found in Spalteholz'[23] atlas. Corning's drawing shows that the medial wall of the cavernous sinus is thin and trabeculated and composed of tissue-thin walled venous channels. The outer wall of the sinus is thick and tough dura. In Morris' anatomy[41] it is stated: "The inner wall (of the cavernous sinus) is practically absent the blood spaces communicating across the midline with the opposite sinus." The ocular and trigeminal nerves and the carotid artery course through the loosely trabeculated and blood-filled sinus. In view of the frailty of the medial wall of the cavernous sinus and its direct apposition to the hypophysis, it seems curious that pituitary adenomas do not give evidence of invasion of the cavernous sinuses more often than

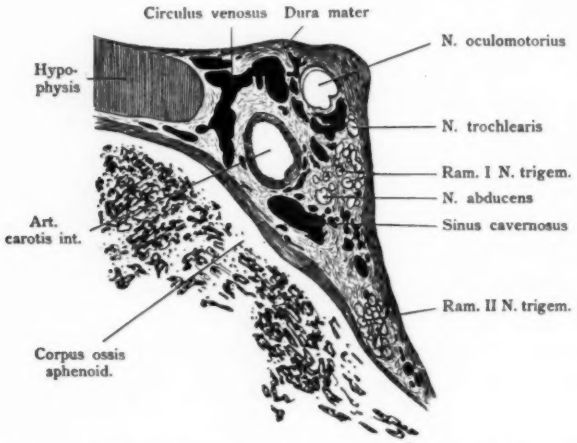

Fig. 10.—Coronal section taken through the center of the hypophysis. The relative positions of the ocular and trigeminal nerves are shown, although it is to be remembered that they vary from body to body. The important fact, well shown here, is that the thin sinusoidal wall of the cavernous sinus is opposed to the hypophysis and forms its lateral boundaries. It can easily be seen how a pituitary adenoma expanding laterally would meet no resistance in implicating the nerves. It is also obvious that as the floor of the sella turcica is deepened by the tumor, more and more of the medial wall of the sinus comes into relation with the tumor. The vulnerable position of the third nerve and the more sheltered position of the sixth are well illustrated. (From Corning.[40])

they do. It may be that lateral growth of tumors is more common than supposed but that the very weakness of this inner wall operates in some cases to produce the opposite effect by yielding and bending before the tumor and thus avoiding implication of the nerves. It is

41. Morris, H.: Human Anatomy, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1905.

interesting that on roentgenographic grounds Schüller[42] came to the same general conclusion expressed in his remark: "Since there are no lateral walls to the pituitary fossa, a tumor can exist for a while without appreciable alteration" [of the sella].

Another point of importance concerning the relation of the hypophysis and cavernous sinus is that it is evident from the anatomic structure of the parts that expansion of the bony sella turcica and deepening of its floor progressively brings more and more of the tumor into apposition with the medial wall of the cavernous sinus. In view of the intimacy of this relation, the occurrence of relatively few cases in which paralysis of structures contained in the cavernous sinus existed would seem to show that a favorable combination of circumstances is required to produce these effects. In other words, the lateral direction of growth is most likely to occur when heavy dorsum sellae and anterior clinoid processes are present, when the sellar diaphragm is thick and resistant and when the medial wall of the cavernous sinus is fragile.

In only early cases, of course, will the lateral growth of the tumor be most apparent at the time the specimens are studied. Eventually a pituitary adenoma must escape the confines of the sella turcica, either posteriorly or vertically. Therefore, in certain cases by the time operation or autopsy is performed the original situation is partly obscured by growth in several directions. This would be most true in rapidly growing tumors. The early stage of the lateral mode of growth was observed in cases 1, 2 and 12 in which small nodules of laterally extending tumor were found at the operating table. They appeared in these cases lateral to the carotid artery or lateral to the optic nerve. In case 4, as the photograph shows, the tumor had extended far out into the middle fossa, although its vertical growth was exceedingly small. Another point is brought up in the study of this case. Since these tumors in growing laterally tend to undermine the cavernous sinus and grow into the middle fossa by stripping up the dura from the base of the skull, the extent of lateral growth would also seem to be limited or facilitated by the tightness or looseness of the attachment of the dura to the base of the skull. An excellent illustration of a pituitary adenoma insinuating itself between the dura and the base of the skull as it grows laterally from the pituitary fossa may be found in Heuer's article.[37] On the other hand, in cases 3 and 5 the tumors had apparently grown rampantly from the time the first symptoms referable to implication of the structure contained in the cavernous sinus were noticed. In case 13 the postmortem protocol was regrettably brief, but the tumor was described as being tightly adherent to the carotid arteries, which we take to mean that there had been considerable lateral extension of the

42. Schüller, A.: The Sella Turcica, Am. J. Roentgenol. **16**:336, 1926.

tumor. A rapidly growing adenoma may obscure the operative interpretation of the cause of the disturbances referable to the ocular nerves and the nerve trigeminal, since it is difficult to visualize this region when a superimposed tumor mass intervenes. This was true in cases 3 and 5. Careful dissection of the autopsy specimens showed, however, how the early symptoms were produced by encroachment into the cavernous sinuses.

Once the tumor has escaped laterally and impinged on the medial walls of the cavernous sinus, the paralyses produced will depend on the absolute and relative positions of the various contained structures. The position of the carotid artery and the nerves varies considerably between persons. The arrangement shown for instance in figure 10 is by no means constant. The internal carotid artery may form its S-shaped loop immediately as it emerges from the anterior lacerated foramen, or it may form it far anteriorly in the sphenoid fissure or anywhere between. Thus whatever buffering protection it may afford the nerves varies with the position of the carotid loop as well as with the point at which the tumor first protrudes and also with the anterior or posterior position of the sella turcica in the sphenoid bone. The relative position of the nerves to one another as well as their absolute position varies considerably as pointed out by Sluder.[24] The sixth nerve, according to Sluder, which ordinarily lies low and laterally may course high in company with the fourth nerve. The third nerve, as figure 10 shows, is relatively exposed, particularly anterior in the sphenoid fissure, which probably accounts for its frequent implication. While it ordinarily lies high in the cavernous sinus and is exposed to the penetration of a tumor, Sluder found that in some instances it occupied a low position in the sinus.

If the sella turcica lies relatively far back in the sphenoid bone and the carotid artery forms its loop anteriorly, a tumor extending laterally would be in a favorable position to impinge on the sixth nerve as it enters the cavernous sinus through Dorello's canal. In 2 of the 4 cases in which the sixth nerve was the only ocular nerve affected (cases 6 and 9) there were erosions of the petrous apexes clearly demonstrable. This suggests that it is at this point that the sixth nerves are involved.

It is probable also that the various divisions of the fifth nerve are impinged on by the lateral growths when they tend to extrude more posteriorly. This is also suggested by the fact that in 3 of the 4 cases in which the sixth nerve was the only ocular nerve involved (6, 9 and 14) the fifth nerve was involved along with it.

To sum up, the irregular way in which the various nerves are involved is only accountable on the basis of individual peculiarities in the position of the nerves contained within the sinus and possibly on irregularities in the growth of the tumor which are in turn determined by anatomic differences in the position and structure of the sella turcica.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The combination of palsy of the ocular nerves and pain in the trigeminal field obviously points to a lesion in the region of the sphenoid fissure. The only difficulty that arises in cases presenting this combination of symptoms is a determination of the nature of the lesion. It is important to realize the other diagnostic possibilities that may produce the same picture.

Before the differential diagnosis is considered, it is important to point out that in addition to the aggregation of signs and symptoms pointing to implication of the structures contained in the cavernous sinus, the cases reported here presented two fairly constant characteristics: (1) evidences of dysendocrinism and (2) roentgen evidences of an intrasellar lesion. In groups 2 and 3 the additional presence of impaired visual functions suggested pituitary tumor. Regardless of the latter fact the early appearance or the magnitude of the disturbances referable to the ocular and trigeminal nerves cast doubt on the diagnosis of pituitary adenoma.

The conditions to be differentiated are: (1) suprasellar tumor; (2) aneurysm of the internal carotid artery; (3) meningioma of the lesser wing of the sphenoid bone; (4) nasopharyngeal carcinoma with extension through the base of the skull; (5) tumor of the gasserian ganglion; (6) sarcoma of the sphenoid bone; (7) orbital tumor; (8) syphilis and syphilitic arachnoiditis, and last though not least, (9) suppurative sphenoiditis associated with periostitis of the sphenoid fissure.

1. In so far as the symptoms of involvement of the endocrine system and the cavernous sinus are concerned, suprasellar tumors of the hypophysial duct may exactly mimic the clinical picture produced by primary pituitary adenoma. The differential diagnosis must be made on other indirect and often insecure evidence. The most reliable distinguishing characteristics are the roentgen findings. In cases of suprasellar tumor the anterior and posterior clinoid processes and the dorsum sellae are eroded from above downward, so that the final effect is a shallow "dished" appearance of the sella turcica. According to Kornblum,[43] widening of the entrance to the pituitary fossa is an early sign. Moreover, the almost constant occurrence of calcifications within these tumors can be demonstrated roentgenographically as opacities lying above or above and behind the sella turcica. Definite erosion of the floor of the sella turcica is uncommon. However, there are instances in which none of these criteria are absolute, and the proper diagnosis must await exploration.

2. Clinically, aneurysm of the internal carotid artery offers the greatest difficulty in differential diagnosis. Judging from the cases

43. Kornblum, K.: Alterations in the Structure of the Sella Turcica as Revealed by the Roentgen Ray, Arch. Neurol. & Psychiat. **27**:305 (Feb.) 1932.

described by Jefferson,[44] the confusion would be greatest with the subclinoid variety. The onset of severe pain in the trigeminal territory followed quickly by palsy of the ocular nerves is almost typical of aneurysm in the anterior part of the circle of Willis. Yet in 2 of our cases (1 and 7) this was the mode of onset of the clinical picture. However, with aneurysm, the apoplectic onset is almost invariably associated with bloody spinal fluid, the consequence of a minor rupture of the aneurysmal wall and subarachnoid hemorrhage. In the case of the slowly expanding aneurysm which has not "leaked" the differential diagnosis must depend largely on the roentgen findings. Sosman and Vogt,[45] who established the roentgenographic criteria of aneurysm of the internal carotid artery, outlined the syndrome of calcified curvilinear shadows arching above the sella turcica or the presence of an eggshell ring of calcification, unilateral erosion of the body of the sphenoid bone and the anterior and posterior clinoid processes and absence of enlargement of the sella turcica. In addition to these, Jefferson [44] added erosion of the carotid canals and erosion of the optic canals as occurring frequently. As a further point, the absence of evidences of dysendocrinism in cases of aneurysm serves to differentiate them from cases of pituitary adenoma. In Jefferson's series of cases of aneurysm there were no endocrine symptoms. Furthermore, in none of his cases was there the expanded and ballooned sella turcica that was so characteristic of the cases here described. Occasionally audible bruits may be detected in cases of aneurysm.

3. Meningioma of the lesser wing of the sphenoid bone may also give considerable difficulty in differential diagnosis since palsy of the ocular nerves, pain in the trigeminal field, visual field defects and occasionally proptosis constitute the cardinal symptoms. According to Cushing and Eisenhardt,[46] Alpers and Groff,[47] and Groff,[48] such tumors almost routinely produce either exostoses or erosions of the lesser wing of the sphenoid bone. The tumor is slow growing, and the development of the symptoms is slow. While lateral erosions of the sella turcica are common, the expanded sella turcica found in cases of pituitary

44. Jefferson, G.: Compression of the Chiasm, Optic Nerves and Optic Tracts by Intracranial Aneurysms, Brain **60**:444, 1937.

45. Sosman, M. C., and Vogt, E. C.: Aneurysms of the Internal Carotid Artery and the Circle of Willis from a Roentgenological Viewpoint, Am. J. Roentgenol. **15**:122, 1926.

46. Cushing, H., and Eisenhardt, L.: The Meningiomas, Springfield, Ill., Charles C. Thomas, Publisher, 1938.

47. Alpers, B. J., and Groff, R. A.: Parasellar Tumors: Meningeal Fibroblastomas Arising from the Sphenoid Ridge, Arch. Neurol. & Psychiat. **31**:713 (April) 1934.

48. Groff, R. A.: Syndrome of Meningeal Fibroblastoma Arising from the Lesser Wing of the Sphenoid Bone, Arch. Ophth. **15**:163 (Feb.) 1936.

adenoma is not seen. Groff stated that disturbances pointing to suppression of pituitary function are occasionally seen, but these cases are the exception. He further pointed out that failing vision is the most common initial complaint and that the disturbances referable to the ocular and trigeminal nerves appear later.

4. Nasopharyngeal carcinoma and lymphoepithelioma, the latter the so-called Schmincke tumor, frequently by extension through the base of the skull manifest their presence by a combination of pain in the trigeminal zones and paralysis of the ocular nerve. Not uncommonly in addition to the symptoms already mentioned, visual impairment and defects of the visual field occur. According to the studies of Needles,[49] Schlivek[50] and of Woltman,[51] who have examined large numbers of patients with such growths, evidences of dyspituitarism are uniformly lacking. Roentgen examination of the skull in 14 of the 20 patients studied by Needles showed various erosions of the base of the skull and of the body of the sphenoid bone. The frequent presence of enlarged cervical lymph nodes and the high incidence of aural complaints, 50 per cent according to Needles, may give the clue to the diagnosis. Pallor, loss of weight and cachexia were commonly present. In spite of these differentiating criteria, Woltman reported a case in which operation was done for pituitary tumor because of the presence of visual loss, field defects and destruction of the sella turcica. Operation disclosed a malignant tumor of the sphenoid mucosa. Needles referred to a case in his series in which for a time the diagnosis was thought to be pituitary adenoma.

5. Tumor of the gasserian ganglion may grow large and impinge medially on the structures in the cavernous sinus. Such growths have been referred to by Frazier,[52] Peet,[10] and Davis and Martin.[53] Clinically they may resemble a lesion in the sphenoid fissure. They can be differentiated from pituitary adenoma with lateral growth by the fact that endocrine disturbances are lacking and also because they do not produce the alterations in the sella turcica characteristic of intrasellar tumor. Moreover, as we have found in our experience, views of the base of the skull frequently show erosion of the foramina ovale and

49. Needles, W.: Malignant Tumors of the Nasopharynx with Special Reference to the Neurological Complications, J. Nerv. & Ment. Dis. **86**:373, 1937.

50. Schlivek, K.: Ocular Manifestations of Malignant Tumors of the Nasopharynx: Report of Cases, Arch. Ophth. **17**:1055 (June) 1937.

51. Woltman, H. W.: Malignant Tumors of the Nasopharynx with Involvement of the Nervous System, Arch. Neurol. & Psychiat. **8**:412 (Oct.) 1922.

52. Frazier, C. H.: An Operable Tumor Involving the Gasserian Ganglion, Am. J. M. Sc. **156**:483, 1918.

53. Davis, L., and Martin, J.: Surgical Lesions of the Para-Trigeminal Area, J. A. M. A. **113**:1952 (Nov. 25) 1939.

rotundum. Cohen,[54] however, published a case of tumor of the gasserian ganglion in which the sphenoid fissure was markedly eroded, as demonstrated roentgenographically. The changes were similar to those occurring in our case 11. Furthermore, field defects were present in his case. On the whole, however, the differential diagnosis will not cause much trouble, since there is usually a history of pain, dysesthesia and anesthesia of long duration preceding the development of other signs. As a last resort, the encephalographic demonstration of air in the chiasmal cistern will exclude at least the possibility of hypophysial tumor.

6. Sarcoma of the sphenoid bone can produce all of the signs and symptoms of involvement of the structures contained within the cavernous sinus. The differential diagnosis will depend on the presence of widespread destruction of the sphenoid bone and the base of the skull visualized by roentgen examination coupled with the absence of the expanded and ballooned sella turcica. The association of dyspituitarism with these rapidly growing malignant tumors would be unlikely. Moreover, agonizing pain is the rule. Nasopharyngeal masses may occasionally be found on appropriate examination.

7. Intraorbital tumor may occasionally simulate a tumor of the hypophysis by extending back into the middle cranial fossa. Proptosis, palsy of the ocular nerves, atrophy of the optic nerve, visual impairment and unilateral field defects may all be found and may on occasion lead to the diagnosis of a parahypophysial or hypophysial tumor. Groff [48] cited a case of Grant's in which an intraorbital tumor mimicked a meningioma of the lesser wing of the sphenoid bone. However, the marked erosion and dilatation of the optic foramen in cases of intraorbital tumor will serve to differentiate them in most instances from pituitary adenoma. Moreover, the absence of dysendocrinism and the absence of the expanded sella turcica will direct attention away from the hypophysis as the source of the symptoms.

8. Syphilis and basal arachnoiditis, like syphilis anywhere, may cause disturbances resembling the ones in the cases under discussion. The results of serologic tests as well as pleocytosis of the spinal fluid easily establish the diagnosis. The danger does not lie in syphilis being mistaken for laterally growing pituitary adenoma but in the adenoma being mistaken for syphilis. Roentgen studies of the sella turcica should make the situation clear.

9. Chronic sphenoiditis associated with periostitis of the sphenoid fissure offers less diagnostic difficulties, although this condition may simulate the pituitary adenomas described here. As shown by Onodi,[33]

54. Cohen, I.: Tumors Involving the Gasserian Ganglion, J. Nerv. & Ment. Dis. **78**:492, 1933.

Sluder,[55] Canuyt and Terracol,[34] the sphenoid sinuses may form the inferior and medial wall of the optic canals, and the sinus will be separated from the optic nerve by only an eggshell thickness of bone. In some persons dehiscences in the walls of the sinuses allow the mucous membrane to be in direct contact with the optic nerve. The sphenoid air cells may extend far out into the greater wings of the sphenoid bone to underly the gasserian ganglion. Under favorable circumstances infection in the sphenoid sinus may manifest itself by palsy of the ocular nerves, due to an associated periostitis of the sphenoid fissure, visual loss, visual field defects and pain in the trigeminal field. While the optic neuritis resulting from infection can usually be distinguished from compression of the optic nerve, de Schweinitz [56] has pointed out that in some cases compression of the optic nerve begins with a macular or paramacular scotoma, so that differentiation on perimetric examination alone cannot always be made. Cases of ophthalmoplegia and pain in the trigeminal field have been reported by Onodi,[33] Thomsen,[57] Panas,[58] Hoffman, de Lapersonne and Stanculéanu,[59] Baumgartner,[60] and de Lapersonne [61] and Post.[62] However, washings from the sphenoid sinus and the history of a preceding nasal infection, along with the absence of alterations in the sella turcica, should lead to the correct diagnosis.

Since so many varied conditions may cause identical signs and symptoms, it is obvious that the cases in which there is involvement of the structures of the cavernous sinus must be thoroughly studied with all available means. The reason for this discussion of the differential diagnosis is mainly to add to the conditions to be differentiated the possibility that a pituitary adenoma may be responsible for the symptoms.

SURGICAL IMPLICATIONS

It is now the generally accepted principle, as Horrax [63] recently pointed out, always to approach the pituitary adenoma from the right

55. Sluder, G.: The Relations of the Sphenoid Sinus to the Semilunar Ganglion and Their Possible Clinical Importance, Tr. Am. Laryng. A. **38**:276, 1916.

56. de Schweinitz, G. E.: Concerning Certain Ocular Aspects of Pituitary Body Disorders, Mainly Exclusive of the Usual Central and Peripheral Hemianopic Field Defects (Bowman Lecture), Tr. Ophth. Soc. U. Kingdom **43**:12, 1923.

57. Thomsen, cited by Onodi.[33]

58. Panas, cited by Onodi.[33]

59. Hoffman, de Lapersonne and Stanculéanu, cited by Onodi.[33]

60. Baumgartner, cited by Onodi.[33]

61. de Lapersonne, F.: Des complications orbitaires et oculaires des sinusites, Bull. et mém. Soc. franç. d'opht. **19**:1, 1902.

62. Post, cited by Onodi.[33]

63. Horrax, G.: Surgery of Pituitary Tumors, A. Research Nerv. & Ment. Dis., Proc. (1936) **17**:665, 1938.

side when performing transfrontal craniotomy. This procedure is adopted because it is technically much easier for a right-handed operator to approach from the right. Another consideration is the avoidance of the left-sided speech centers. This is especially important if it becomes necessary to resect the frontal lobe to gain exposure of the tumor. It appears that this justifiable standardization of technic requires amendment in the cases of tumor that present the syndrome of the cavernous sinus on the left side. Judging from the operative findings in the cases reported here and the necropsy observations, the approach must be from the side presenting the disturbances referable to the ocular and trigeminal nerves if relief is to be obtained. In 2 of our cases, however, the sellar diaphragm had not ruptured, and the tumor had apparently been deflected laterally, since it was not able to expand vertically. Since this circumstance may possibly exist, the indications for the selection of the side of operation should also depend on the evidences of predominant lateral erosion of the sella turcica as shown on the roentgen films.

Since these tumors may occupy and infiltrate the cavernous sinus, extreme care must be taken to avoid tearing the sinus, with resultant uncontrollable hemorrhage. This catastrophe occurred in case 4. Unless a definite capsule can be distinguished in the laterally extending portion of the tumor it is probably unwarranted to attempt to remove it. Removal, when attempted, should always be within the capsule. It is questionable whether any further effort should be made to remove the capsule, since it is usually inextricably bound up with the cavernous sinus.

Radiation seems to have a fairly good effect in relieving symptoms referred to involvement of the nerves contained in the cavernous sinus. This is indicated by the disappearance of the palsy of the ocular nerves in cases 10 and 14 after roentgen treatment. However, the cases reported in this series show the difficulties and dangers of any attempt at surgical extirpation when the tumor has escaped from the sella turcica. The recent insistence on roentgen therapy as a primary treatment for pituitary adenomas should be reconsidered in this light.[64] If roentgen therapy rather than surgical intervention is used as the initial attack on a pituitary adenoma and is unsuccessful, the tumor may spread widely, thus making a surgical attack difficult and hopeless if occasion demands it later on.

SUMMARY

Fourteen cases of primary pituitary adenoma are described which presented unusual neurologic and neuro-ophthalmologic clinical pictures. They were divided into three groups: (1) those in which the disturbances

64. Grant, F. C.: The Surgical Treatment of Pituitary Adenomas, J. A. M. A. **113**:1279 (Sept. 30) 1939.

referable to the ocular and trigeminal nerves comprised the exclusive neurologic picture; (2) those in which the symptoms referable to the ocular and trigeminal nerves dominated the clinical picture but in which there were some evidences of implication of the optic chiasm, and (3) those in which the disturbances referable to the ocular and trigeminal nerves were an important part of the clinical symptoms but in which there were unequivocal visual field defects indicating an intrasellar lesion.

The disturbances referable to the ocular and trigeminal nerves in these cases were accounted for by the implication of the cavernous sinus. It was shown that occasionally pituitary adenomas grow laterally and that this mode of growth may produce the clinical picture of a lesion in the sphenoid fissure rather than the classic chiasmal syndrome.

The anatomic structure of the sella turcica and its surroundings which result in the lateral growth of the tumors with involvement of the structures contained in the cavernous sinus were discussed.

The conditions to be differentiated from the pituitary adenoma were considered.

The changes in the usual surgical technic when a lateral extrusion of a pituitary adenoma has been diagnosed are discussed.

ABSTRACT OF DISCUSSION

Dr. William J. German, New Haven, Conn.: The essayists have made an important contribution in emphasizing this subsidiary syndrome of pituitary adenoma. At the suggestion of Dr. Francis Grant, I reviewed some of Dr. Cushing's cases of pituitary adenoma with this syndrome in view, selecting 50 consecutive cases out of a series of 327. I was surprised at first to find that in 24 there was significant subjective or objective palsy of the ocular nerves (exclusive of unequal pupils) or involvement of the fifth nerve. In 10 of these 24 cases palsy of the ocular nerves or involvement of the fifth nerve was present at the onset of symptoms. In other words, the neural involvement initiated the clinical syndrome. In 4 of these 24 cases visual symptoms were not present at the onset. In other words, at the onset of the symptoms the syndrome was exclusively that of the cavernous sinus, which these authors have described. Finally, in 1 of the 50 cases visual symptoms were not present even at the time of operation.

There has been a tendency for a good deal of emphasis to be placed on the roentgen appearance of sella turcica. However, in the 50 cases that I reviewed the sella turcica was not significantly enlarged in 6 of that group.

Ptosis, which the authors mentioned, was present in 2 of the cases, and the trigeminal portion of the syndrome was prominent in 5 cases, with severe pain. Involvement of the motor fibers of the trigeminal nerve was noted in 3 patients.

From the anatomic standpoint, 2 cases were of some interest. In 1 case resection of the trigeminal roots was done, and the laterally placed pituitary adenoma was verified at that operation. The operation, of course, was done because of extreme pain.

The second case was interesting from a standpoint of autopsy, and I quote: "On both sides of the enlarged cyst the third nerve and the ophthalmic portions of the fifth nerve were closely implanted in the lesion of the cavernous sinus. The carotid arteries were lying against the tumor." In spite of the close proximity of the ophthalmic division of the fifth nerve, this patient had no pain referable to the trigeminal nerve, although there was diplopia.

Dr. Oscar Hirsch, Boston: Brain surgery, which originated in Europe, has been improved in an admirable way by Cushing and his pupils and some other neurosurgeons in the United States. I participated in this problem by developing a new approach to the hypophysis by the intranasal way. Local anesthesia is used. From one incision on the septum the mucous membrane is dissected as far as the anterior wall of the sphenoid bone. The same procedure is carried out on the other side of the septum. Then the anterior walls of the sphenoid cavities are exposed and opened. The enlarged sella turcica becomes visible and its bone is removed. After excision of the dura, the tumor is removed by using the curet or suction.

I have operated in 336 cases, with a mortality rate of 5 per cent. To prevent relapses, radium is applied directly to the sella turcica. This procedure is used as a routine measure for all solid tumors, which, because of the size or location, cannot be removed completely. Permanent improvement has been achieved in the majority of the cases, some of the patients being followed for twenty years.

The advantage of this method is that no external scar is visible, that there is no exposure of the brain and that the patients endure only a small amount of discomfort.

Concerning the actual problem brought up by these authors, I have to add that the syndrome of the cavernous sinus is seldom seen at the onset of a tumor of the pituitary body, and if it appears, it may lead to an incorrect diagnosis. I operated on a surgeon suffering from a pituitary tumor, but at the onset there was ptosis of the lid. The roentgen findings were not definite. The patient was therefore treated for basal syphilitic meningitis for several years till he lost his sight. The operation could not restore his sight, but the patient lived for six years or longer.

The syndrome of the cavernous sinus is not so rare in cases of malignant pituitary tumor or in cases in which the pituitary tumor has not been treated and in the advanced stage propagated toward the lateral wall. There it compresses or infiltrates the sinus cavernosus and the nerves in its surroundings.

Dr. Paul C. Bucy, Chicago: I should like one of the authors to explain briefly how the differentiation has been made clinically in the first cases that he reported between intracranial aneurysm, which so closely resembles pituitary adenoma and pituitary adenoma.

Dr. Francis H. Adler, Philadelphia: In answer to the last question, the main point of differentiation must be, of course, the constitutional symptoms, and primarily they are those of pituitarism.

CARCINOMA OF THE LACRIMAL SAC

REPORT OF A SECOND CASE

CHARLES N. SPRATT, M.D.
MINNEAPOLIS

During the past year I have observed a second case of primary carcinoma of the lacrimal sac. The carcinoma in this case was much more advanced than in the case reported by me [1] in 1937.

History.—Mr. C. F. C., aged 66, consulted me on June 12, 1939. He stated that about five years previously he had been troubled with lacrimation of the left eye. About the same time a swelling appeared beneath the skin at the inner angle of the eye. This swelling gradually increased, and the eye was pushed forward and toward the temporal side. He had diplopia; a gradual loss of the vision followed. In the last few months he had considerable pain.

Examination.—There was considerable proptosis of the left eye, which was pushed forward and toward the temporal side (fig. 1 *A*). The motion was limited in all directions. Over the lacrimal sac there was a hard rounded mass, approximately 1.5 cm. in diameter. The lower lid was swollen, and there was a hard, somewhat lobulated, mass occupying the inner two thirds. The conjunctiva was edematous, and the blood vessels were engorged. Beneath the conjunctiva on the superior nasal and inferior portions was a hard flattened mass, which was adherent to the sclera. The skin was nowhere red or broken and was adherent to the mass only in the region of the lacrimal sac. The vision in the left eye was 20/100. With the exception of the enlargement of retinal vessels, the fundus was normal. The left antrum was dark on transillumination. The left naris was normal on inspection.

Operation.—With the patient under ether anesthesia, the entire contents of the orbit were removed en masse. In order to do this, it was first necessary to make a wide canthotomy incision. The periosteum of the orbit was incised at the superior, nasal and inferior margins. This was then elevated as far back as the apex. The optic nerve was cut, and the mass was rotated forward, the lacrimal sac finally being freed with the tumor mass (fig. 2). The lacrimal bone came away with the tumor. It was also found that the floor of the orbit was softened and that the tumor had extended into the antrum. The lining of the antrum, which was much thickened, was removed with a curet. The wound was packed and allowed to fill with granulations.

Sections were sent to Dr. Fredrick H. Verhoeff, who reported as follows:

"The slide labeled 'H 039 373 antrum' [fig. 3] shows a papillary epidermoid carcinoma. The tumor is invading the lymph spaces but is not infiltrating the tissue. The cell masses are surrounded by basement membranes. In a few places in the section there are remains of normal ciliated epithelium of mucous membrane.

"Such tumors may arise from accessory sinuses. There are three tumors in our pathologic collection which occurred in the region of the lacrimal sac. All

1. Spratt, C. N.: Primary Carcinoma of the Lacrimal Sac, Arch. Ophth. **18:** 267-273 (Aug.) 1937.

of these are similar to your tumor. I have also seen sections of a papillary epithelioma which arose from a canaliculus, but I am unable to find them now.

"The other section labeled 'Mr. C., carcinoma of the lacrimal sac' [figs. 4 and 5] shows an extremely malignant carcinoma invading and infiltrating striated muscle. This is probably an epidermoid carcinoma, but owing to its rapid growth, its exact

Fig. 1.—Patient before (*A*) and after operation (*B*).

Fig. 2.—Drawing of the eye and orbital contents. There is a small stick in the lacrimal sac showing the portion removed for the section depicted in figure 4.

classification is uncertain. In places there is much new formed fibrous tissue pervaded by narrow irregular strands of tumor cells, producing a picture closely resembling that of a scirrhous carcinoma of the breast. This appearance could have been produced by radiation treatment if such treatment had been used in this case. There is nothing in this specimen to prove the origin of the tumor from the lacrimal sac or duct.

"If the two specimens you sent me are from the same case, it is astonishing that the same tumor could grow in such different forms."

The patient was referred to Dr. Walter H. Ude for high voltage roentgen therapy. The patient was treated from June 26 to Aug. 25, 1939, a total of sixty days. He was not treated from July 5 to 17. A total of twenty-six treatments was given. The number and distribution of fields were: anterior orbit, direct, and lateral left orbit and sinus. The doses per field were: 2,500 roentgens to the lateral field and 2,600 roentgens to the direct anterior field. The total dose was: 5,400 roentgens, 2,200 being given from June 25 to July 5 and 3,200 from July 17 to August 25. Two hundred kilovolts were used at a constant potential.

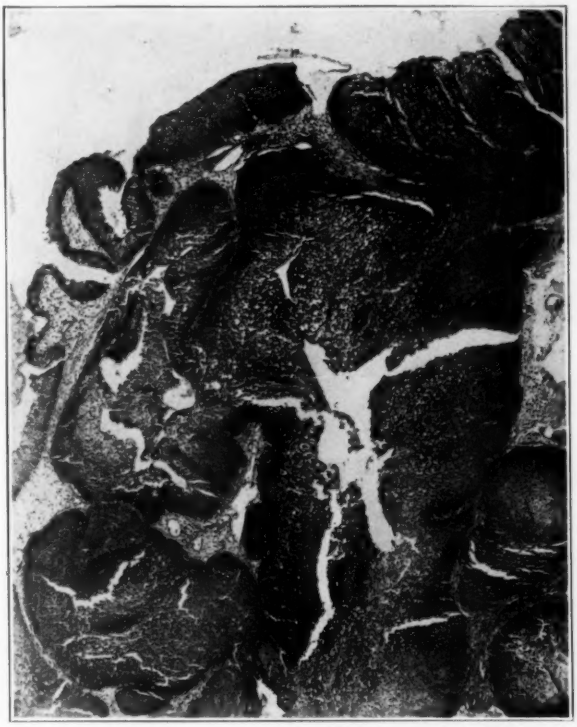

Fig. 3.—Section from the lining of the antrum.

This dose is at the upper limit of the tolerance of the skin at the present time. Treatment had to be discontinued during the course because of an acute reaction to the orbit.

It is now nearly ten months since the operation, and the patient has increased in weight and there are no signs of recurrence. The skin over the left cheek is somewhat reddened due to the roentgen treatment (fig. 1 *B*).

The history and progress of this case closely parallel those of my first one, which was observed from the onset. A swelling was noted over the lacrimal sac, and there was epiphora. After the removal of

the tumor, there was a recurrence in the lower lid. Later the growth extended over the sclera and back of the globe.

The case described by Landau likewise resembles my second case. A brief report follows:

A man, aged 67, two months before the first examination had a severe cold, and immediately afterward there was lacrimation of the right eye. Four weeks prior to the first examination the patient noticed a small hardened mass in the right inner angle of the eye.

Fig. 4.—Cross section of the lacrimal sac; low power.

Clinical and roentgen examination showed a hardened mass, the size of a lentil, in the right nasolacrimal duct. There was little sense of irritation.

A diagnosis of probable malignant neoplasm was made. Operation was urged, but the patient refused.

Five months later the patient returned and presented the following picture: The right palpebral fissure was markedly narrower than the left; there was marked edema of the lower lid and the inferior palpebral conjunctiva. The bulb was displaced upward and outward. The tumor now occupied more than a third of the lower orbital edge and extended into the depths. Again the patient delayed operation, and, finally, seven months after the first examination, he made up his mind to submit to the clearly indicated operation.

Histologic examination showed cylindric epithelium covered with mucosa, the stroma of which showed chronic inflammatory infiltration and was found to contain numerous tiny seromucous glands.

REVIEW OF THE LITERATURE

In my former report on primary carcinoma of the lacrimal sac, I collected 17 cases from the literature. Penman and Wolff [2] reported a case of malignant papilloma of the lacrimal sac and listed 64 cases of primary malignant tumor of the sac, among which were 24 cases

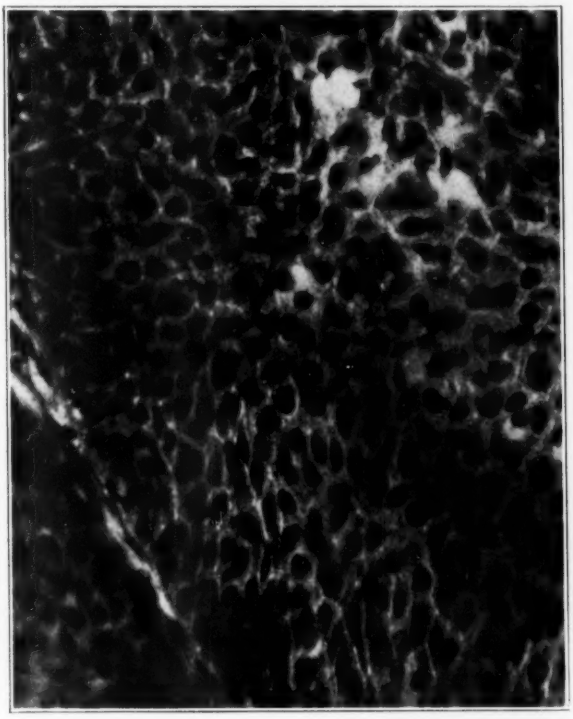

Fig. 5.—High power magnification of the section shown in figure 4.

of cancer. Three of these were reported in personal communications, 1 each by Jones, Noble and Stallard. One case included in this series as a carcinoma is credited to Cabannes. I was not able to get Cabannes' original article, but Azzena [3] stated:

2. Penman, G. G., and Wolff, E.: Primary Tumors of the Lacrimal Sac, Lancet **1**:1325-1328 (June 11) 1938.

3. Azzena, P.: Tumori dell'occhio, Pavia, Tipografia cooperativa, 1923, pp. 284-288.

Cabannes published the account of a sarcoma extending to the nasal fossae, but since it was of the pavement cell type the author claimed that it had taken origin in the epithelium of the lacrimal canals.

McCool [4] reported a case he called one of mixed cell tumor of the lacrimal sac. He stated:

The picture presented was that of a mixed-cell tumor similar to those so frequently seen in the salivary glands (myxochondroepithelioma).

Diagnosis.—Mixed-cell tumor of the lacrimal sac. As soon as the malignant character of the lesion was established from the pathologic report, the patient was referred to Dr. Laurence Taussig, who implanted radium in the cavity from

Synopsis of Additional Cases of Carcinoma of the Lacrimal Sac

Case No.	Author Year	Sex, Age	Side	Duration	Diagnosis	Treatment	Result
18	Seggel [5] 1884	♂ ?	Rt.	Epiphora for years	Papillary epithelioma	Excision	Cure
19	Šťasník [6] 1928	♀ 42	Lt.	6 mo of lacrimation; tumor for 2 wk.	Carcinoma, pavement cell	Excision, radium and roentgen rays	Well 10 mo.
20	Sená [7] 1932	♂ 37	?	Mucocele removed short time before	Epithelioma	Excision	Unknown
21	Sená [7] 1932	♂ 37	Lt.	Lacrimation for 6 mo.; mucocele recurred in 3 mo.	Epithelioma	Removal; radium and roentgen rays	Well 8 mo.; no recurrence
22	Halbertsma [8] 1933	♀ 68	Rt.	Rapid growth for 3 to 4 wk.	Cylindric carcinoma	Operation; roentgen rays	Well a few weeks
23	Landau [9] 1933	♂ 67	Rt.	2 mo.	Cylindric epithelioma	Removed in fragments	Unknown
24	Jones [2] 1938	..	....	.....	Carcinoma	Removed	?
25	Noble [2] 1938	♂ 58	....	10 yr.	Carcinoma	Diathermy	.....
26	Stallard [2] 1938	.. 60	....	.....	Carcinoma	.....	.....
27	Spratt 1940	♂ 67	Lt.	5 yr.	Carcinoma	Operation; roentgen rays	Well 14 mo.

which the tumor had been removed. I saw the patient ten months after the operation and there had been no recurrence. I realize, however, that so short a time does not preclude the possibility of a recurrence, but inasmuch as I have not seen the patient since, I am unable to say whether there have been any metastases or whether the patient is still living.

The abstracting department of the American College of Surgeons has checked the literature and has made abstracts from original articles. I find additional cases reported by Seggel,[5] Šťasník,[6] Sená,[7]

4. McCool, J. L.: Mixed-Cell Tumor of the Lacrimal Sac, Am. J. Ophth. **22**:734-743 (July) 1939.

5. Seggel: Bericht über die Augenkrankenstation des Königlichen Garnisonlazarths München, Deutsche mil.-ärztl. Ztschr. **13**:161, 213, 271, 325 and 399, 1884.

6. Šťasník, E.: Primary Epithelioma of Lacrimal Sac, Časop. lék. česk. **67**: 85-86 (Jan. 13) 1928.

7. Sená, J. A.: Tumores malignos del saco lagrimal, Semana méd. **2**:1042-1049 (Oct. 13) 1932; Rev. Asoc. méd. argent. **46**:1048-1055 (Sept.) 1932.

Halbertsma [8] and Landau,[9] which were not included in my former paper.

DIAGNOSIS, PROGNOSIS AND TREATMENT

All writers agree that in the first stage of the disease, epiphora being the only symptom, diagnosis is not possible. In the second stage of swelling or tumor diagnosis could be made. The presence of a round hard mass not reduced by pressure, especially if fluid passes into the nose on irrigation, thus showing a patent duct, is indicative of thickening of the wall of the lacrimal sac rather than a mucocele. In the third stage, when invasion of the tissue of the lids and orbit has occurred, the diagnosis is apparent. It is only in this stage that pain has been reported.

These tumors are extremely malignant, and recurrence is the rule. Few patients have been under observation long enough to give any information as to the ultimate results. In my first case the patient lived eight years after the first operation and more than four years after the last operation for recurrence. Death was due to coronary thrombosis. Poseys' patient was followed two years, and Bakken and Oudendal's was observed eighteen months.

So far as could be determined, removal was done in all reported cases, and the best result followed the subsequent roentgen treatment. In my first case radium used after the tumor had extended to the orbit was not sufficient, and radical removal was done.

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8. Halbertsma, K. T. A.: A Case of Primary Carcinoma of the Lacrimal Sac, Nederl. tijdschr. v. geneesk. **77**:5200-5204 (Nov. 18) 1933.

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UNUSUAL CHANGES IN THE LENS FOLLOWING TRAUMA

ORIGIN AND TREATMENT

DANIEL M. ROLETT, M.D.
NEW YORK

The 5 cases of post-traumatic stationary cataract to be presented here are unusual in some aspects.

In 2 of the cases there was a history of a perforating injury and in 3 of nonperforating injury. The cataracts in all the cases bore a strong resemblance, the main characteristics being: (*a*) a peculiar cobweb-shaped central opacity involving similar layers of the lens and (*b*) a stationary character.

Perhaps the early age at which the patients were injured had something to do with the formation and development of the cataract. The purpose of presenting these cases is to seek some additional information in regard to the theory of formation of this type of cataract as well as to find the best way of preventing its development once the injury to the eye has occurred. And because so little is known as to what actually happens to the lens in an injury (eliminating those with rupture of the capsule), it is not at all surprising that the slipshod therapy of administering injections of foreign protein or of giving huge quantities of polyvitamins are useless, as they were in my cases, the reports of which follow:

CASE 1.—Ida R., aged 8 years, in an attempt to untie her knotted shoe lace with the aid of scissors suddenly cut her right eye. The accident occurred in January 1932, and the patient was seen by me in June 1932.

Physical examination revealed a poorly nourished child with enlarged cervical glands and infected tonsils. The Wassermann reaction was negative and the Mantoux test positive.

Examination of the injured eye (right) showed an absence of photophobia, but the eye was extremely sensitive to examination and readily became injected and teared. The lids and the palpebral and bulbar conjunctiva were normal. Faint pericorneal injection was noticeable.

The cornea showed a thin, vertical, penetrating scar, of about 5 to 6 mm., on the temporal side, bisecting the space between the pupillary border and the temporal limbus. The scar was about 2 mm. wide in the center, and toward each end became very pointed. After penetrating the cornea, the scar formed a bridge

Read before the Section of Ophthalmology of the New York Academy of Medicine, Feb. 19, 1940.

in the anterior chamber uniting the cornea with the lens. The anterior surface of the lens showed a thick scar penetrating the lens to Bowman's membrane. Peripherally it was surrounded by a delicately outlined, cobweb-shaped opacity,

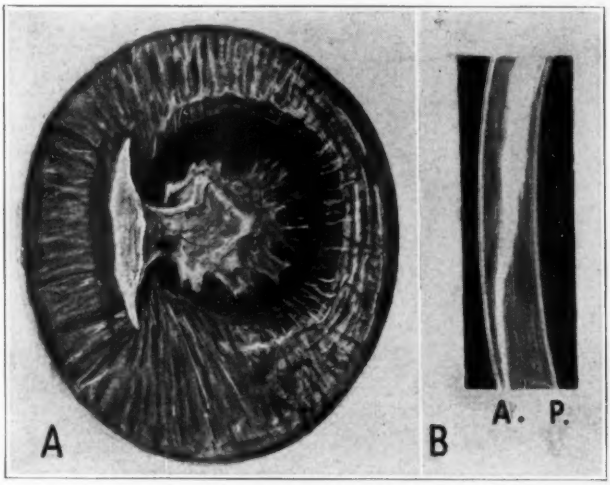


Fig. 1 (case 1).—*A*, appearance of the injured lens when viewed with corneal microscope. *B*, sagittal view of the corneal scar.

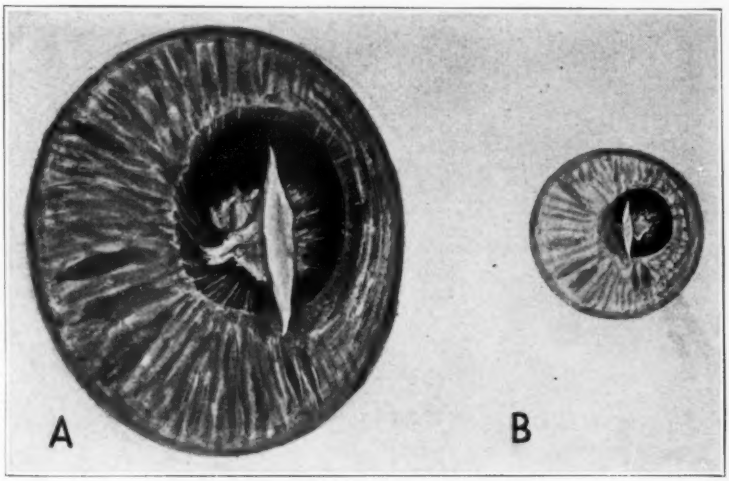


Fig. 2 (case 2).—*A*, appearance of the injured lens when viewed with the corneal microscope; × 5. *B*, same as *A*; × 2.

giving the appearance of a cracked ice surface. A number of newly formed blood vessels traversed the scar. The iris was adherent to the scar on the temporal side, and in the anterior chamber a few occasional cells were seen floating. Deeper media and fundus were seen only with difficulty and poorly.

Vision in the right eye was limited to counting fingers at 1 to 2 feet (about 30 to 60 cm.). Projection of light was good, with some limitation on the temporal side.

Case 2 is strikingly similar to the first one.

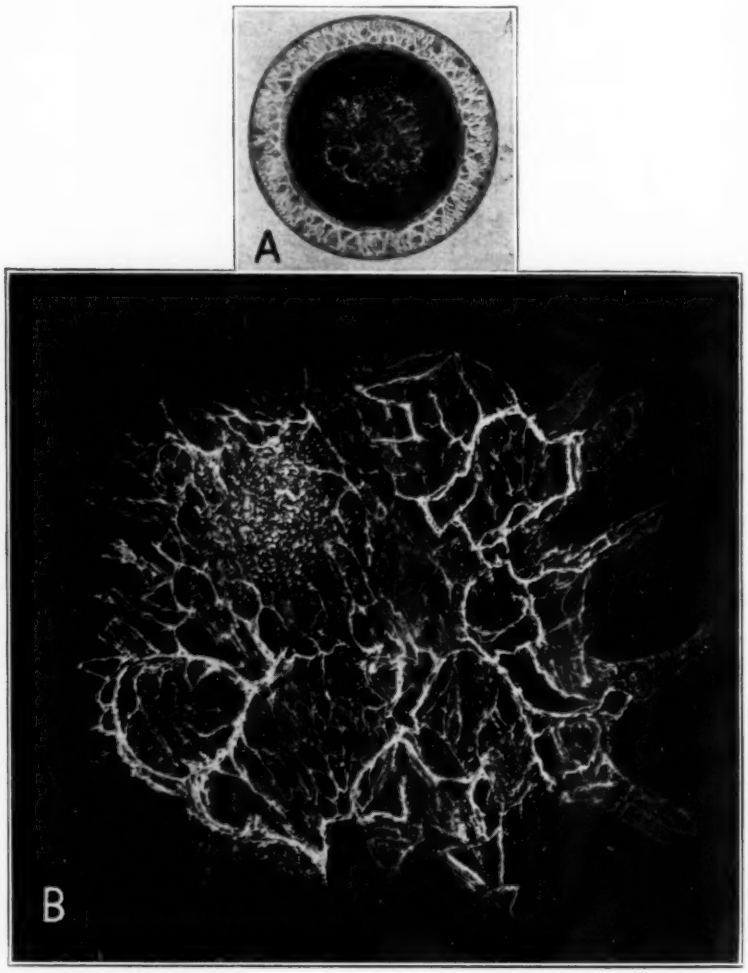


Fig. 3 (case 3).—*A*, appearance of the injured lens when viewed with the corneal microscope; × 2.5. *B*, same as *A*; × 25.

Case 2.—Steven S., aged 13 years, accidentally cut himself in the left eye while whittling with a pocket knife at the age of 8.

Physical examination gave negative results.

The right eye was normal. The cornea of the left eye showed an old penetrating vertical scar, about 4 to 5 mm. in length, located slightly nasally from

the center and penetrating the entire thickness of cornea and the anterior chamber; in the lens it was abruptly stopped by Bowman's membrane. The iris was adherent to the scar, and the pupil was drawn in. The temporal margin of the pupillary border was denuded of the epithelium, exposing the underlying pigment, and a few newly formed blood vessels traversed from the scar into the iris stroma.

Surrounding the scar in the lens was a peculiar cobweb-shaped opacity; it did not extend beyond Bowman's membrane and involved the central part of the lens.

The fundus could not be seen, and vision amounted to counting of fingers at 4 feet (120 cm.).

Case 3.—Ernst L., aged 15 years, was first seen by me in 1931. He gave a history of trauma to the left eye. As an infant he bumped this eye against the

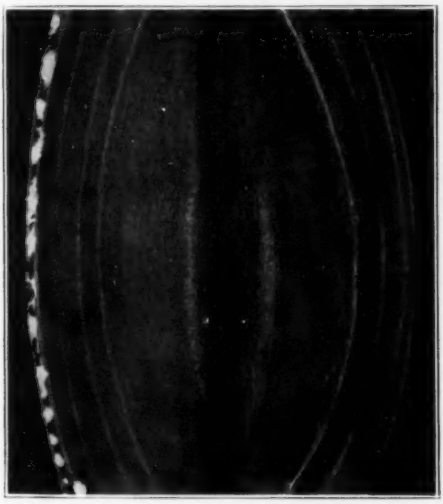


Fig. 4 (case 3).—Optical section of the lens.

corner of a table. Vision has since been poor, but he is more conscious of the defect at present.

Physical examination revealed a well developed, red haired boy, with no signs of congenital defects.

The Wassermann and the tuberculin tests were negative.

Examination of the right eye gave negative results. Vision was 20/70; with a -1.00 sph. $\bigcirc$ -0.50 cyl., axis 90 it was 20/20.

External examination of the left eye gave negative results. The cornea and the anterior chamber were normal. The lens showed a central opacity of beautiful cobweb design, which when viewed with the Zeiss binocular microscope appeared to lie on the surface of the lens. An enlargement of 25 times showed the opacity to consist of a delicate framework supporting a fine dustlike opacity, which toward the periphery ended in sharply pointed processes. This opacity at no point penetrated deeper than Bowman's membrane. The fundus was seen only with difficulty and appeared to be normal. Vision was limited to counting fingers at 3 feet (90 cm.).

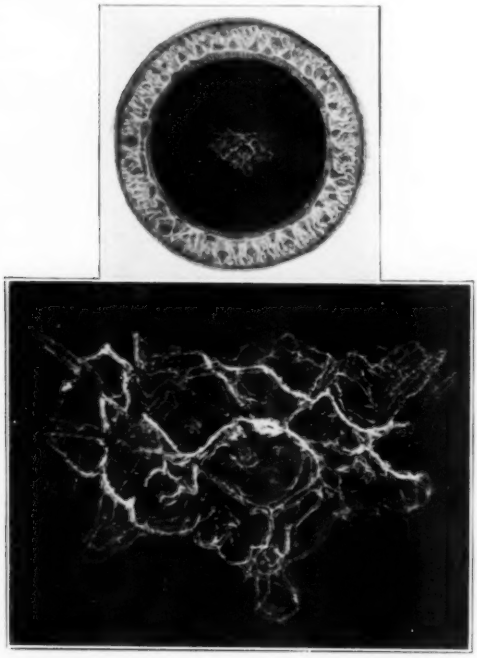


Fig. 5 (case 4).—Frontal view of opacity of the lens.

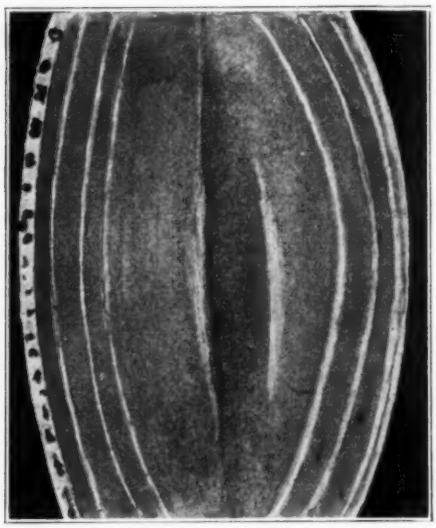


Fig. 6 (case 4).—Optical section of the lens.

CASE 4.—Peter S., aged 5 years, was seen by me in 1936. His parents noticed that the right eye in certain light showed a small opacity in the pupil. They gave the following history: At the age of 3½ years, while swinging a metal toy on a string, the child struck himself in the right eye. The eye was red and painful for about two weeks, during which time it was seen and treated by the family physician several times. The eye appeared to heal normally. Several months later, however, the mother noticed for the first time a spot in the boy's eye. At present it seems to her to be definitely larger.

Physical examination revealed a perfectly normal and well developed child.

The Wassermann and tuberculin tests were negative.

Examination of the right eye revealed a small central opacity in the lens, remarkably similar to the one described in the previous case. Perception of light was perfect. The vision was limited to counting of fingers at 3 to 4 feet.

The left eye was normal. Vision was 20/20.

CASE 5.—Israel L. was struck in the right eye with a ball while playing football. The accident occurred on Sept. 24, 1939. He was seen by me three days later at the New York Eye and Ear Infirmary. Dr. Clyde McDannald suggested that I follow up this case.

At the first examination the injured eye was red and painful and teared profusely. The center of the cornea had a small abrasion, and the rest of the cornea was somewhat hazy and edematous. In the anterior chamber a small hyphema was noticeable. A number of cells and fibrin were likewise present in the anterior chamber, which was somewhat deeper than normal. The iris was swollen and turgid, covered with small clots of blood, and the pupil was more than midway dilated and reacted sluggishly to light, although a marked spasm of the orbicularis muscle was noticeable. The anterior surface of the lens had a definite shagreen appearance and a fine film over the surface, the details of which could not be seen because of the difficulty in keeping the eye open.

Vision at this time amounted to counting of fingers at 4 feet.

One week later the injured eye showed marked improvement. The corneal abrasion healed entirely, and the anterior chamber was clear of blood and fibrin. There was still a great number of freely moving cells in the anterior chamber. The anterior surface of the lens showed the fine film still unchanged. At this time the question of an exudate arose. The deeper media and the fundus were seen with difficulty. There was a question of edema of the disk owing to the blurred outline of the disk. Vision was 20/70.

One month later the following fully defined picture presented itself: External examination gave negative results. The anterior chamber was perfectly clear, with the excepton of one or two detected cells. The iris appeared normal. The pupil was midway dilated (atropine), and the lens showed the same, by now, familiar cobweb-shaped opacity, appearing to lie on the anterior and also on the posterior surface of the lens. In both instances it invaded the epithelium and subepithelium, almost reaching Bowman's membrane on the anterior surface and Descemet's membrane on the posterior surface. The opacity involving the posterior capsule showed an unusual depression inward. At the periphery of this opacity a number of pigment cells were embedded.

The anterior structure of the vitreous showed an increased density in its supporting structure.

The fundus, which at this time could not be seen well, appeared to be normal.

Vision in the right eye amounted to 20/40.

Fig. 7 (case 5).—Cataractous changes on the anterior surface of the lens.

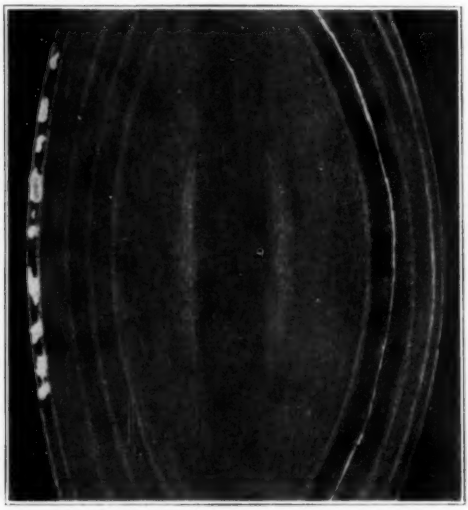


Fig. 8 (case 5).—Optical section of the lens, showing changes on the anterior surface.

The interesting point in this case was that although the peculiarly shaped opacity on the anterior surface of the lens appeared to be an exudative membrane lying on the surface of the lens, actually it was an opacity penetrating beyond the capsule and reaching as far as the first disjunction band. That it may have started as an exudate is not only not denied but is verified by the fine threadlike connections between the opacity and the iris. These bands were distinctly not congenital. The posterior surface of the lens showed a fine webby structure occupying the greater part of the center of the pupil, with minute openings running in the same direction as the webby fibrils of which the opacity was made up. The central depressed structure ended in irregularly shaped processes pointed in different directions and almost reaching the periphery of the lens. The left upper quadrant showed a number of minute pigment cells clustered on the surface of the lens without any supporting structure. This opacity of the posterior surface of the lens was not connected with that of the anterior surface and involved the capsule and subcapsular layers.

ORIGIN AND TREATMENT

It is hard to explain this type of cataract, even considering the seriousness of the injury to the eye. The questions that arise in my mind, and this will also explain my reason in presenting these cases, are the following:

1. Assuming that the cataract is due to the injury, is it due to trauma to the lens capsule, and if so, even with no evidence of rupture, is the injury severe enough to alter the permeability of the capsule?

2. Is the cataract due to sudden and violent change in the shape of the lens, especially in the region of the anterior and posterior poles, thereby disrupting and damaging the delicate lens fibrils?

3. Is the cataract due to direct trauma to the ciliary body and iris, thereby, indirectly affecting the nutrition of the lens?

Discussing these questions one by one, the first one in which it is assumed that the lens capsule has been injured must be rejected, otherwise one would have evidence that the posterior corneal surface coming in contact with the lens injured it. For lack of evidence of injury to the posterior corneal surface, it must be assumed that no such contact has occurred. Furthermore, nowhere is there evidence of the pupillary imprint on the lens surface, which certainly would have occurred simultaneously.

The second question must be likewise rejected, because such violent injury as to rupture or cause disjunction in the lens fibers in the anterior and especially in the posterior polar region would almost surely show evidence of a break in the capsule as well. Likely the delicate fibrils

Fig. 9 (case 5).—Cataractous changes on the posterior surface of the lens.

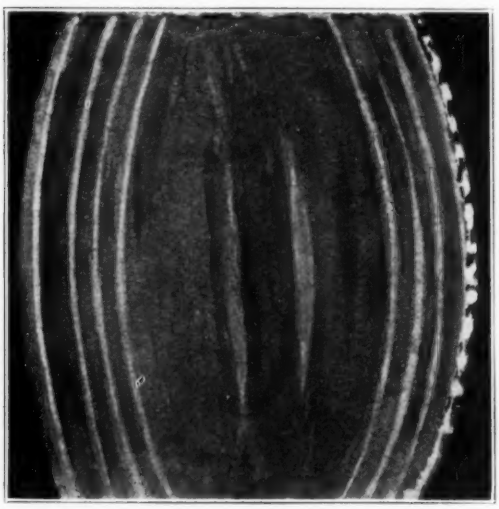


Fig. 10 (case 5).—Optical section of the lens, showing changes on the posterior surface.

of the suspensory ligament as well as of the vitreous adjoining the lens would also have been damaged or ruptured. In my case, with the exception of some questionable thickening of these fibrils, no other change occurred in the vitreous, the consistency remaining perfectly normal. There was no evidence of damage to the suspensory ligament.

Therefore, the factor presented in the third question (involvement of the ciliary body and iris) must be considered as the possible cause of the cataract.

To substantiate this possibility further, it should be remembered that the injury to the eye, at least in 1 case, resulted in a corneal abrasion, accompanied by far too great circumcorneal injection and photophobia to account for the comparably slight injury to the cornea. On the other hand, there is direct evidence of injury to the iris: the presence of blood in the anterior chamber, as well as cells and fibrin, and an edematous iris and a turgid, slow reacting pupil. The early presence of a fine film (perhaps an exudate) on the surface of the lens will tend to verify the serious trauma to the ciliary body as well. And finally, the threadlike adhesions between the lens and the iris should not be forgotten.

Assuming, then, that there is some truth in this supposition, I am perhaps not at all wrong in advancing the following theory of formation of this traumatic cataract. This theory consists of the probability that following the injury to the eye traumatizing the iris and ciliary body, an exudate accompanying the hemorrhage into the anterior chamber spreads either over one or over both surfaces of the lens. This exudative membrane, which I thought I could see early after the injury, in 1 case had a chance to become organized at the poles. At the periphery of the lens it could not do so, because of the more active circulation of the aqueous humor which washed the periphery of the lens more vigorously and therefore swept the membranous exudate away before it had a chance to organize. Similarly, when blood is artificially injected into the anterior chamber filling it, there remains a small central clump of blood cells adhering to the anterior pole of the lens long after every other trace of blood disappears.

Once this exudative membrane has time to organize, it is not difficult to presume that it interferes with osmosis and permeability of the lens vital to its life and transparency. The opacities remain local because comparatively only a small portion of the lens is involved and the deeper structures are not injured either directly or indirectly. How else can one explain the identical changes in the lens at the anterior and posterior poles, leaving the periphery of the lens clear and free of any changes?

Perhaps this would also explain the apparent futility of treating persons with such injuries with injections of foreign protein or with large doses of polyvitamins.

On the other hand, if there is something to my theory, then it would be logical to try to treat persons with such traumatic injuries very early by repeated punctures of the anterior chamber, thereby forcefully increasing the flow of the aqueous and allowing it to wash away all the exudative and other debris resulting from the injury. Unfortunately, this method occurred to me some time after the last patient was discharged and it was too late to do anything about it. I cannot at any rate see any danger in carefully puncturing the anterior chamber at the limbus, and there may be a possibility, no matter how exaggerated it may seem now, that in some cases of traumatic cataract this type of treatment may prove effective, thereby saving the invaluable sight of the injured.

DISCUSSION

DR. FRANK E. MALLON: May I ask the approximate time between the occurrence of the accident and the recognition of the lenticular changes?

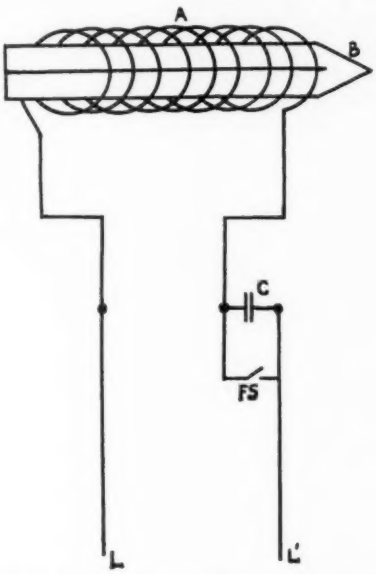
DR. DANIEL ROLETT: In the case referred by Dr. McDannald it took about four weeks. In this case I could see the changes on the anterior surface of the lens as well as on the posterior surface. Unfortunately I did not see the patients in the other cases until at least a year after the injury.

Clinical Notes

A METHOD OF ELIMINATING ARCING IN THE FOOT SWITCH OF AN EYE MAGNET

MYRON DRACHMAN, M.E., AND BENJAMIN FRIEDMAN, M.D., NEW YORK

In using the old type giant eye magnet for removing intraocular foreign bodies, a disconcerting electric arc and a crackling noise emanate from the foot switch, accompanied by smoke resulting from the burning of the switch contacts. This requires frequent cleaning of the contacts,



Apparatus for eliminating arcing in the foot switch of an eye magnet. *A* indicates magnet coils; *B*, magnet core; *C*, condenser; *FS*, foot switch, and *L* and *L'*, power line, direct current, 110 volts.

and at times replacement of the affected parts may be necessitated. A more important consideration is the annoyance to the operator and the frightening effect on the patient.

The physical principles involved in producing these undesirable manifestations are simple, although measurement and calculation are rather complex mathematically. The coil of the magnet is supplied by a direct current, and this creates a powerful magnetic field in the core. When the current is broken, the sudden collapse of this field generates, by self induction, an extremely high voltage, which instantly flows back along the "lead in" wires and jumps the gap which is produced as the switch opens. This volatilizes the metal of the switch contacts and

causes an arc, which is equally damaging to the switch mechanism and the equanimity of the patient and the operator.

In order to overcome these objectionable effects, we employed a condenser mounted across the switch terminals. This condenser by-passes the electric surge harmlessly around the switch as it is being opened, since the condenser offers little resistance to this transient current. By the time the switch is fully opened, the current surge has dropped to zero. The condenser has the property of blocking any inflow of direct current to the magnet.

In selecting the proper condenser for this purpose, one should know the inductance value of the magnetic coil in use. The capacitive reactance of the condenser should equal the inductive reactance of the coil for complete quenching of the arc. In our own case, the inductance of the coil was approximately 4.5 henries, and we found a condenser of 2 microfarads rated at 600 volts to be satisfactory. No noticeable arc occurred on breaking the current.

A further advanage of this arrangement is that it enables one to use a small convenient foot switch instead of the old and cumbersome heavy type. It is possible to interpolate at moderate cost a similar condenser in the circuit of any existing eye magnet where an unwelcome arc occurs.

A SIMPLE METHOD OF TREATING DACRYOCYSTITIS IN THE NEWBORN

ARCHIMEDE BUSACCA, M.D., SÃO PAULO, BRAZIL

For several years I have been using irrigations of Besredka filtrates in the treatment of catarrhal and purulent dacryocystitis of adults. While results have not been brilliant, because it is possible in only a certain number of cases to restore the patency of the nasolacrimal canal, I have, however, not given up their systematic trial, for even in the cases of failure one can diminish the purulent secretion. I have the impression that the after-care of the disease is always shortened, possibly on account of the state of immunization which develops in the tissues.

I have been following the same treatment for nearly three years in the dacryocystitis of the newborn, and the good results obtained in 6 cases leads me to offer the following communication:

The irrigation of the lacrimal sac is done each time with about 2 cc. of bouillon containing the Besredka filtrates. I have always obtained the restoration of the lumen of the nasolacrimal canal with this method.

The technic is simple. After anesthetization with cocaine, a fine and delicate blunt cannula is introduced into the lower lacrimal point. If the cannula is too large for the canal, a conical probe is first used to dilate it. As soon as the cannula is introduced into the lacrimal sac, the liquid contained in the syringe is injected with as much pressure as possible.

The irrigations are repeated every second day. They do not produce any reaction, and only rarely is there any edema, in which case one allows a greater interval between treatments.

In general, few injections are necessary to restore the opening of the canal. As soon as the purulent secretion is diminished, this opening may frequently be obtained by a simple maneuver. While one is performing the irrigation, one compresses with a finger the inner third of the upper lid against the bone of the nose in order to prevent the fluid escaping from the sac by way of the upper canaliculus. One thereby increases the hydraulic pressure existing in the sac, and this is often sufficient to open the nasolacrimal canal immediately.

When there is a great deal of discharge, a larger number of irrigations is necessary, and it is not until the secretion is greatly diminished or has stopped that one can succeed in opening the duct. The inflammatory edema causes the walls of the canal to stick together, and it is not until this inflammation has subsided that the hydraulic pressure can overcome the resistance in the lower part of the nasolacrimal duct.

In short, good results depend on the two following features: the action of the filtrates which cures the inflammatory process by local vaccination and the action of the hydraulic pressure which overcomes the resistance offered by the valve in the canal or by a nonpatent canal.

The method is to be recommended because of the constancy of its results, its ease of application and the fact that it does not produce injury.

Correspondence

MEASUREMENT OF THRESHOLD INTENSITY

To the Editor.—I should like to call attention to an error which appeared in the article by Drs. Isaacs, Jung and Ivy in the October issue of the ARCHIVES (**24:** 698, 1940), entitled "Clinical Studies of Vitamin A Deficiency."

In their graphs of data obtained on the Hecht-Shlaer adaptometer the threshold intensities are given logarithmically in terms of micromillilamberts. This is incorrect. Their normal data fall in a range similar to the range observed by Dr. Selig Hecht and myself; the correct unit of light intensity is the micromicrolambert (1 micromicrolambert is equal to $\frac{1}{1,000}$ micromillilambert, or one billionth of a millilambert). Their intensities of brightness are in error, therefore, by 3 log units.

Incidentally, they gave a wrong reference when quoting from the paper by Dr. Hecht and myself; their footnote 28 should read: Hecht, S., and Mandelbaum, J.: The Relation Between Vitamin A and Dark Adaptation, *J. A. M. A.* **112:** 1910-1916 (May 13) 1939.

J. MANDELBAUM, M.D., Brooklyn.

CORRECTION

In the article by Drs. Robb McDonald and Francis H. Adler entitled "Clinical Evaluation of Tests of Dark Adaptation," in the September issue (ARCH. OPHTH. **24:** 447, 1940), the basal metabolic rates mentioned in the twenty-first and twenty-second lines on page 459 should read "+ 80" and "+ 100" instead of "— 80" and "— 100."

News and Notes

SOCIETY NEWS

Pan-American Congress of Ophthalmology.—Pan-American relationships took another step forward in the field of medicine when the Pan-American Congress of Ophthalmology was organized on a permanent basis at the meeting of the first congress in Cleveland, Oct. 11 to 12, 1940, under the auspices of the American Academy of Ophthalmology and Oto-Laryngology.

Dr. Harry S. Gradle, Chicago, was elected president of the congress. Drs. Conrad Berens, New York, and Moacyr E. Alvaro, São Paulo, Brazil, who served with Dr. Gradle as members of the committee that organized the initial meeting, were elected executive secretaries.

The following vice presidents were elected: Drs. S. Hanford McKee, Montreal, Canada; Frank E. Brawley, Chicago; Edward Jackson, Denver; Thomas R. Yanes, Habana, Cuba; A. Vasquez-Barriere, Montevideo, Uruguay; Jose Pereira Gomes, São Paulo, Brazil, and Enrique Demaria, Buenos Aires, Argentina.

There will also be a council, which is to be formed by one representative from each of the twenty-one American republics. The representative from each country is to be elected by the national ophthalmologic society or societies, if such exist; if there is no such society, the government of the country will be asked to appoint a member of the council.

Montevideo was tentatively selected as the place of the next meeting, to be held in 1943.

Eighteen delegates, representing governments, universities, hospitals and medical societies in Brazil, Chile, Costa Rica, Cuba, Colombia, Guatemala, Panama and Puerto Rico, were present in Cleveland. An extensive program of scientific papers was presented, about equally divided between English, on the one hand, and Spanish and Portuguese, on the other. English papers were discussed by Latin-American speakers; those in Spanish or Portuguese, by English-speaking physicians.

The language difficulty was overcome successfully by the use of slides. Extensive summaries of the papers were projected on the slides in Spanish or Portuguese for the English ones, or in English for those given in the other languages.

Earlier in the week the Latin-American delegates were guests of the American Academy of Ophthalmology and Oto-Laryngology at its scientific sessions and at the annual banquet, where each was formally introduced. At the Pan-American banquet, held Friday night, October 11, the guests from Latin America all expressed appreciation and enjoyment of the meeting. It was the general impression that the congress had brought about better understanding among the ophthalmologists of the western hemisphere. It was felt that the Latin Americans were impressed by the meetings of ophthalmologists in this

country and those of the United States were in turn impressed by the scientific ability and skill of the Latin Americans.

At the conclusion of the meeting the Latin Americans left to attend special clinics that were being held in their honor at some of the large ophthalmologic centers of the East and Middle West.

American Academy of Ophthalmology and Oto-Laryngology.—Dr. Ralph Irving Lloyd, Brooklyn, was named president-elect of the American Academy of Ophthalmology and Oto-Laryngology at the annual meeting in Cleveland, Oct. 6 to 10, 1940. Vice presidents elected were Drs. Everett L. Goar, Houston, Texas; James M. Robb, Detroit, and Ralph O. Rychener, Memphis, Tenn. Dr. Frank R. Spencer, Boulder, Colo., will be president during the coming year.

Dr. William P. Wherry, Omaha, was reelected executive secretary-treasurer and Dr. Secord H. Large, Cleveland, comptroller. The board of secretaries was reelected, as follows: Drs. William L. Benedict, Rochester, Minn., for ophthalmology; John L. Myers, Kansas City, for otolaryngology; Erling W. Hansen, Minneapolis, for public relations; Dean M. Lierle, Iowa City, for instruction in otolaryngology, and Albert D. Ruedemann, Cleveland, for instruction in ophthalmology. Dr. Oliver E. Van Alyea, Chicago, was reelected director of the scientific exhibit.

The academy sponsored the first Pan-American Congress of Ophthalmology.

The place of the 1941 meeting of the academy was not to be determined until later.

North Carolina Eye, Ear, Nose and Throat Society.—Dr. Milton R. Gibson, Raleigh, N. C., was elected president of the North Carolina Eye, Ear, Nose and Throat Society at its annual meeting in Winston-Salem, N. C., Sept. 26, 1940. Dr. Thomas C. Kerns, Durham, N. C., was made vice president and Dr. Vanderbilt F. Couch, Winston-Salem, N. C., secretary. The society voted to require that henceforth applicants for membership must have passed examinations of the American Board of Ophthalmology or the American Board of Otolaryngology.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Biochemistry

CARBONIC ANHYDRASE IN NORMAL AND CATARACTOUS LENSES. A. BAKKER, Arch. f. Ophth. **140:** 543, 1939.

Carbonic anhydrase is an enzyme which catalyzes the breaking up of bicarbonate into carbon dioxide and water and thereby facilitates the carrying away and the elimination of carbon dioxide. The lenses of normal rats contain this enzyme in a surprisingly high concentration. In the galactose cataract of rats the carbonic anhydrase content of the lenses becomes markedly reduced. A relation between the metabolism of the lens, which even in the presence of oxygen is largely a glycolytic one, and the presence of the large amounts of carbonic anhydrates is suspected.

P. C. KRONFELD.

Cornea and Sclera

DEGENERATIVE LIPOID DYSTROPHY OF THE CORNEA. P. PICILLO, Ann. di ottal. e clin. ocul. **67:** 721 (Oct.) 1939.

Twelve cases of fatty degeneration of the cornea were found in the literature. The author reports 2 cases. The first was that of a woman aged 20 who had noted an opacity of the right cornea for eight months. The yellow patch was astride the inner limbus, extending half way to the pupil. The slit lamp localized the opacity in the deeper layers of the cornea. Chemical analysis of the blood showed an increase in total lipoids and in cholesterol. Sections of the excised opacity showed an irregular, vacuolated structure of the anterior half of the cornea; the deeper layers showed densely packed deposits of fatty material between lamellae which were changed in structure so as to give the impression of fibroblasts. Lymphocytes and polymorphonuclear leukocytes were numerous between the fibers. A number of vessels were seen in the deeper layers. The second case was that of a woman of 62, with the history of a corneal ulcer five years before. Scars of healed trachoma and a yellowish opacity in the lower part of the cornea, measuring 5 by 3 mm., were present. The opacity was removed with the trephine, the defect being covered by a conjunctival flap. The epithelium was irregular, and Bowman's membrane was replaced by fibrous tissue. Fat stains showed globules of lipoid material in the basal cells of the epithelium and between the connective tissue cells of the deeper layers. The fact that the patients in 12 of 14 cases in the literature were women suggests a possible endocrine origin of the disease. Two colored illustrations and two photomicrographs are included.

S. R. GIFFORD.

Experimental Pathology

THE ROLE OF BRUCELLA IN HUMAN AND ANIMAL OCULAR DISEASE WITH SPECIAL REFERENCE TO PERIODIC OPHTHALMIA IN HORSES. E. L. BURKY, R. R. THOMPSON and H. M. ZEPP, Am. J. Ophth. **22:** 1210 (Nov.) 1939.

Periodic ophthalmia, "moonblindness" or recurring uveitis, in horses is described and discussed, especially in regard to the etiologic factor. Several cases are cited, and experiments on rabbits and guinea pigs were performed. The following summary is given:

"Brucella (species undetermined) has been recovered at necropsy from the ovaries and milk of three mares sacrificed because of blindness due to clinical periodic ophthalmia. A fourth strain has been recovered from the milk of a mare with a similar ocular condition.

"When injected into the anterior chamber of rabbits or intravenously into rabbits and guinea pigs, the first strain that was recovered produced in some but not all animals ocular inflammation resembling periodic ophthalmia in horses and chronic recurrent intraocular inflammation in humans.

"It is suggested that, because of the experimental results and clinical observations made in the field, infection with Brucella may be the cause, or one of the causes, of periodic ophthalmia. In addition, the experimental results, coupled with clinical observations on humans already reported in the literature, suggest that this infection may play an important role in human ocular pathology." W. S. REESE.

EXPERIMENTAL PRODUCTION OF CONJUNCTIVITIS WITH STAPHYLOCOCCI. J. H. ALLEN, Am. J. Ophth. **22:** 1218 (Nov.) 1939.

Allen calls attention to the lack of success in producing conjunctivitis with living staphylococci as compared to that from the staphylococcus filtrate or toxin. Following experiments to determine the factors involved, he makes the following conclusions:

"1. Toxigenic strains of staphylococci were capable of producing conjunctivitis when instilled onto the normal human conjunctiva.

"2. Conjunctivitis did not develop in infants whose antitoxin titer was more than 0.5 unit per cubic centimeter of serum.

"3. Trauma, either mechanical or toxic, shortened the incubation period of the experimental conjunctivitis in infants.

"4. A nontoxigenic strain of Staphylococcus albus did not produce conjunctivitis in infants.

"5. Conjunctivitis was not produced in rabbits by instillations of staphylococci upon the normal or abraded conjunctiva or when instilled simultaneously with toxin.

"6. In nonimmune rabbits intrameibomian inoculations of toxigenic strains of staphylococci produced an acute meibomitis and conjunctivitis of 2 to 3 weeks' duration followed by a chronic meibomitis and conjunctivitis of 6 to 8 months' duration." W. S. REESE.

General Diseases

THE OPHTHALMOLOGICAL COMPLICATIONS OF LEONTIASIS OSSEA. S. PHILPS, Brit. J. Ophth. **23:** 729 (Nov.) 1939.

A man aged 33 eleven years previously had first had his attention called to the distortion of his head by his physician. Five years later left-sided headaches developed. For some years he has required large-sized hats. Since 1938 his headaches have incapacitated him for work. There was a bony mass occupying the parieto-occipital area and thickening of the left frontal bone, which caused the left orbit to be displaced downward. Vision was 6/6, and the visual field remained normal. Media and fundus were normal. A linear osteotomy of the skull bones was done to relieve the headaches. There was entire relief for two months, when they recurred. The removed bone had the appearance consistent with that found in osteitis fibrosa.

The article is illustrated.

W. ZENTMAYER.

Glaucoma

HEREDITARY GLAUCOMA. P. J. WAARDENBURG, Arch. f. Ophth. **139:** 662, 1939.

Two families in which glaucoma occurred as a hereditary familial disease are described in detail. In some members of one family the glaucoma occurred in the inflammatory form and in others in the compensated form. In the other family the glaucoma was associated with a congenital anomaly in the region of the iridocorneal angle.

P. C. KRONFELD.

RETINAL DETACHMENT IN A CASE OF HYDROPHTHALMOS. T. A. VOS, Arch. f. Ophth. **139:** 691, 1939.

The patient in the case reported in the paper under review was first seen at the age of 1 year. The diagnosis of bilateral hydrophthalmos was made, and several anterior sclerotomies were performed on each eye, the tension apparently becoming controlled. At the age of 8 the patient sustained a severe injury to the head with a blunt object, with rupture of the right eye, which had to be eviscerated. At the age of 14 the left eye sustained an injury by a blunt object, the only apparent sequela of which was a small iridodialysis near 2 o'clock. When the patient was 30, a retinal detachment developed, which promptly subsided on complete rest in bed. This detachment recurred and receded six times during the ensuing six years. At the time of the seventh recurrence a small horseshoe-shaped retinal tear was found near 2 o'clock and closed by operation. Since then (one year ago) the retina has remained in place. The author considers his case as one of compensated, stationary, but not cured, hydrophthalmos and the retinal detachment as a pure coincidence. The tear probably developed at the time of the injury but remained latent for seventeen years.

P. C. KRONFELD.

Lens

INTRACAPSULAR EXTRACTION OF CATARACT. J. WARSHAVSKY, Vestnik oftal. **15:** 8, 1939.

The indications and contraindications for intracapsular extraction of cataract are discussed. Warshavsky has performed this operation on over 800 patients during a period of eight years (1930 to 1938). He uses Elschnig's method. The capsule is grasped at the lower margin, and the lens is turned 180 degrees. A simple extraction was performed on the majority of the patients (over 60 per cent). If the patient was restless or the pupil could not be dilated to the maximum, or if the patient had only one eye, a combined extraction was done. The vision of the majority of the patients was from 0.4 to 0.9. Detachment of the retina occurred in only 3 persons after the operation. In about 26 per cent there was herniation of the vitreous into the anterior chamber. The contraindications for this type of extraction are: soft, juvenile cataract; intumescent senile cataract; cataract associated with general hypertension, and cataract in glaucomatous eyes. O. SITCHEVSKA.

Methods of Examination

TESTING FITNESS FOR NIGHT FLYING. C. E. FERREE and G. RAND, Am. J. Ophth. **22:** 655 (June) 1939.

Ferree and Rand give the following summary:

"As a part of the routine of night flying, the pilot must look back and forth from the comparatively highly illuminated cockpit and instrument panel to more distant outside objects under very low illumination. The ability to do this quickly and with a satisfactory discrimination of detail is perhaps the most important visual qualification of the night pilot. It involves a change in the adjustment of the eyes for both intensity of light and distance of object. The night flyer has quickly to adapt from light to dark and back again to light as well as at the same time change his adjustment for distance from near to far and back again to near. The time required for this combined action in a suitable test relationship can be measured with the instrument and test method described in this paper.

"The task set by the method described closely approximates that set for the night flyer in his routine performances, more closely than is the case, for example, in the tests recommended in two former papers; namely, the light minimum and the light minimum for the discrimination of detail. These were tests only of important general functions, not specific tests for particular performances. The present test is not only a scientific test of capacity but a specific performance test made under scientific conditions with accurate scientific controls. Speed of adjustment for change of distance of object and change of intensity of light is accurately measured—that for change of intensity of light (speed of adaptation) much more accurately than is possible, for example, with any adaptometer that has yet been devised.

"The instrument described also serves a very important purpose in the general testing program for aviators and for testing ocular and general fatigue. Still further uses of the instrument are noted in the paper."

W. S. REESE.

Neurology

AN INNOCUOUS CLINICAL ENTITY SIMULATING TABES DORSALIS: PUPILLATONIA WITH ABSENT REFLEXES (ADIE'S SYNDROME). J. H. BAILEY and E. SASKIN, Am. J. Ophth. **22:** 499 (May) 1939.

This article describes Adie's syndrome, differentiates it from similar conditions and calls attention to the possibility of its being mistaken for tabes. Two cases are reported.

W. S. REESE.

VISUAL DISTURBANCES ASSOCIATED WITH TUMORS OF THE TEMPORAL LOBE. HAWLEY S. SANFORD and HUGO L. BAIR, Arch. Neurol. & Psychiat. **42:** 21 (July) 1939.

The authors' conclusions, based on the study of 211 verified cases of tumor of the temporal lobe seen at the Mayo Clinic, are as follows:

1. Homonymous hemianopia is the most common visual field defect produced by tumors of the temporal and occipital lobes.

2. Quadrantic anopias are produced much more frequently by tumors of the temporal lobe than by tumors of the occipital lobe.

3. Normal fields occur with approximately the same frequency in cases of tumor of the temporal lobe and in cases of tumor of the occipital lobe.

4. Sparing of the macula occurs in association with both groups of tumors but is much more common and of greater degree with the group of tumors of the occipital lobe. In the cases in which necropsy specimens were available there was no instance of sparing of the macula associated with a tumor of the temporal lobe.

5. There is definite evidence in the study of this group of tumors to indicate that the forward looping of the geniculocalcarine fasciculus, as described by Meyer, actually exists. Lesions which affect this portion of the fasciculus may produce a typical picture of the visual fields, which is of diagnostic value.

6. Incongruous homonymous field defects can be produced by tumors of the temporal lobe which affect either the lateral aspect of the homolateral optic tract or the beginning of the geniculocalcarine fasciculus. In the former case the larger defect is in the field of the homolateral eye; in the latter, it is in the field of the contralateral eye.

7. No concrete evidence was obtained either for or against the presence of a crossing bundle of fibers to allow representation of each half of the retinal macula in both occipital lobes.

8. The presence or absence of choked disks and the equality or inequality of the degree of choking in the two eyes are of no clinical value in deciding on which side of the brain a tumor of the temporal lobe is located. Although with unequal degrees of choking of the disks in the two eyes there is more likelihood of the tumor being on the side of the greater choking than on the opposite side, this criterion is too unreliable to be of any value in lateralization of the tumor.

9. Visual disturbances other than the field defects are of no value in helping to diagnose or lateralize tumors of the temporal lobe.

R. IRVINE.

CONGENITAL FACIAL HEMIHYPERTROPHY WITH OCULAR ANOMALIES: REPORT OF TWO CASES. R. GOZBERK, Ann. d'ocul. **176:** 624 (Aug.) 1939.

Congenital facial hemohypertrophy is a rare condition. The writer gives a report of the work of Sabrazes and Cabannes, who in 1898 found 18 cases in the literature, some of which, however, were rather indefinite. The last case noted was presented before the Société française d'ophtalmologie in 1931.

Gozberk gives the details of 2 cases, illustrated with photographs. One patient was a girl of 10 years and the second a child of 2 years.

The chief details of the subject are summarized—etiology, pathologic anatomy, pathogenesis, symptoms and diagnosis. S. H. McKEE.

Parasites

CUTANEOUS MYIASIS OF THE LOWER LID. ANASTASIO RECO and RAUL PICOLI, Arch. de oftal. de Buenos Aires **14:** 433 (May) 1939.

The occurrence of furuncular myiasis produced by the larva Dermatobia hominis (cyaniventris) is reported. The article is illustrated by photographs and photomicrographs. C. E. FINLAY.

The Pupil

MOTILITY OF THE IRIS AND ITS DISTURBANCE. ESTEBAN ADRIGUÉ, Arch. de oftal. de Buenos Aires **14:** 242 (March) 1939.

This is a review of the present status of knowledge of the anatomic and physiologic relations of the iris and the clinical deductions concerning their disturbance. The following topics are taken up successively: innervation of the iris, with the latest developments on the optic pathways connected with its dilation; pharmacologic tests in relation with the pupil; semeiology of the pupil; reflex and associated movements of the pupil; isolated disturbance of the light reflex; pupillary reactions (reactions to pain and to vestibular and cochlear irritation, oculopupillary reaction psychic reflexes and reflexes to convergence and in accommodation); Adie's syndrome; Pitz-Westphal's orbicular phenomenon; Argyll Robertson pupil, with a discussion of its etiology; absolute pupillary rigidity; internal ophthalmoplegia; paralytic mydriasis, with hippus; isolated contraction to convergence and in accommodation, and semeiology of anisocoria. The paper is supplemented with a rich bibliography. C. E. FINLAY.

Physiology

THE RESPONSE OF THE EYE TO LIGHT IN RELATION TO THE MEASUREMENT OF SUBJECTIVE BRIGHTNESS AND CONTRAST. W. D. WRIGHT, Brit. J. Ophth. **24:** 1 (Jan.) 1940.

This article is essentially a review of the present knowledge of the subjective effects of light. The objective data of Hartline's on single nerve fibers of the optic nerve and the retinal action potentials, which

have been the basis of most of Granit's work, serve as an introduction. The author points out that the subjective measurements of the visual response are difficult because of the impossibility of measuring sensations. There are 11 figures in graphic form dealing with subjective measurements of the visual response, i. e., brightness discrimination and sensitivity of the fovea during light adaptation.

A method of reproducing any apparent brightness is outlined and applied to a test which enables brightness comparisons to be made. This leads up to the author's specification of contrast and the statement that "contrast could then be safely measured in terms of the subjective brightness of the contrasting areas." He believes that the measurement of contrast by the binocular method would obviate many difficulties in the measurement of subjective brightness.

The article has been condensed from another on the same subject by the author and does not permit a more detailed review.

R. McDONALD.

CIRCULATION OF THE AQUEOUS HUMOR. A. CLAVEL, Ann. d'ocul. **176:** 657 (Sept.) 1939.

The problem of the circulation of aqueous humor of the eye is one that has interested oculists for a long time. Despite the large amount of research work, there is as yet no agreement regarding the existence of this circulation and its mechanism. The reports of numerous writers are noted.

The author reports his work under three headings: (1) the source of elimination of the aqueous humor, (2) the source of secretion of the aqueous humor and (3) the action of the muscles of the eye on the circulation of the aqueous humor.

Every time that the intraocular tension rises above the level of the elimination point of the aqueous humor, a certain quantity is discharged from the eye, until the tension becomes normal or below the elimination point.

Every time that the intraocular tension descends below this level, which is variable according to the ocular blood circulation, a certain quantity enters the eye until the intraocular tension becomes normal or above this point.

Contraction of the ciliary muscle makes possible the circulation of the aqueous humor and assures its renewal when the normal movements of the external muscles and of the iris are not in action.

A bibliography accompanies the article. S. H. McKEE.

Refraction and Accommodation

SHALL WE USE CYCLOPLEGICS? W. H. CRISP, Am. J. Ophth. **22:** 392 (April) 1939.

Crisp concludes that the ophthalmologist cannot afford to neglect the advantages to be derived from the use of cycloplegia, although in case of necessity he should be competent to make a noncycloplegic examination with the greatest possible accuracy. W. S. REESE.

ANISEIKONIA. C. BERENS and M. LOUTFALLAH, Am. J. Ophth. **22**: 625 (June) 1939.

Berens and Loutfallah examined 711 hospital patients and 125 private patients for aniseikonia. The iseikonic prescription was worn by 368 patients in group 1 (hospital and private patients) and by 50 patients in group 2 (private patients). In group 1, 73 per cent obtained some relief of symptoms, and in group 2, 74 per cent. W. S. REESE.

Retina and Optic Nerve

EXAMINATION OF THE FUNDUS OF THE EYE DURING THE COURSE OF BLOOD TRANSFUSIONS (VENOUS TENSION). I. BORSOTTI and P. PILLET, Bull. Soc. d'opht. de Paris **51**: 188 (March) 1939.

The authors, under the direction of Bailliart, studied all patients having blood transfusions over a period of time in order to ascertain changes in arterial and venous circulation in the retina. A curious observation was the fact that after receiving 60 cc. of blood a patient who had no spontaneous venous pulse acquired one, which persisted. Neither the arterial tension of the retina nor the general arterial tension were affected by the transfusion. In 12 of the 33 patients observed at the time of transfusion a venous pulsation was noted. In 3 patients a spontaneous venous pulse disappeared after transfusion. The authors theorize that as a rule transfusion causes a local lowering of venous tension. This may be on a basis of active or passive dilatation of the venous system. L. L. MAYER.

SYMPTOMS OF PAPILLEDEMA. ALBERTO URRETS ZAVALIA and ROBERTO OBREGON OLIVA, Arch. de oftal. de Buenos Aires **14**: 152 (Feb.) 1939.

The objective and subjective symptoms of papilledema are studied separately and in detail, with the different methods of examinations and the findings in the different stages.

The paper is illustrated with numerous retinograms and is supplemented with a complete bibliography. C. E. FINLAY.

Retina and Optic Nerve

CAUSATION AND FREQUENCY OF RETROBULBAR NEURITIS. P. CIBIS, Klin. Monatsbl. f. Augenh. **102**: 205 (Feb.) 1939.

In a paper, well illustrated with tables, Cibis renders an account of the etiologic factors in 189 cases of retrobulbar neuritis observed at the ophthalmic clinic of the University of Heidelberg during the last eighteen years. The findings are discussed and compared with those obtained at other ophthalmic hospitals. Acute retrobulbar neuritis was present in 133 cases, multiple sclerosis prevailing, namely, in 56 of these cases, while the etiologic factor remained unknown in 55. In the remaining 22 cases, sinusitis, acute poliomyelitis, grip, infection of the teeth and other acute infections were present. Multiple sclerosis

was suspected in 22 of the 55 cases in which the etiologic agent was not established. After elimination of all those cases in which some other etiologic agent was found, including arteriosclerosis and amblyopia caused by tobacco and alcohol, multiple sclerosis was found to be the cause of retrobulbar neuritis in 70 per cent of the 189 cases. This figure tallies with that of Fleischer (66 per cent) and of Langenbeck (77 per cent). The ages of Cibis' patients ranged between 14 and 78. One of the tables demonstrates that the frequency of retrobulbar neuritis did not increase from year to year correlative with an improved diagnosis but that it varied irregularly. Cibis stresses the predominating frequency of multiple sclerosis as an etiologic factor in retrobulbar neuritis. The frequency of multiple sclerosis observed by Cibis showed a parallelism with the frequency of this disease recorded for the same years at the neurologic hospital at Heidelberg.

K. L. STOLL.

THE VESSEL SYSTEM OF THE FOVEA CENTRALIS. R. SALUS, Acta ophth. **17:** 279, 1939.

In the course of studying the changes of the retinal vessels in arteriosclerosis and hypertension, Salus has become convinced that, contrary to the prevailing opinion, the region of the fovea centralis possesses a complicated but well defined system of vessels. These vessels are minute continuations of the branches arising from the superior and inferior temporal vessels. In young persons they can be traced by careful ophthalmoscopic examination well beyond the region of the foveal reflex, sometimes to the foveola.

These observations have led the author to question another prevalent view, namely, that the foveal region and the neuroepithelium of the rest of the retina depends on the choriocapillaris for its nutrition. He finds the animal experimentation that has been done in regard to this point unconvincing and the clinical observations to furnish fully as much evidence against this conception as for it.

This article concludes with a description of the changes undergone by the vessels in the foveal region as age advances in cases of arteriosclerosis and of hypertension.

O. P. PERKINS.

Trachoma

REACTION OF THE TRACHOMATOUS PATIENT TO A VACCINE MADE OF BACILLUS PROTEUS X 19. V. DERKAC, Arch. f. Ophth. **140:** 502, 1939.

Because of the similarity between trachoma inclusion bodies and rickettsias on the one hand and the relation between Rickettsia prowazeki and Bacillus proteus X 19 on the other hand, the author studied the local and systemic reactions of trachomatous and nontrachomatous patients to intracutaneous and subcutaneous injections of a vaccine made of Bacillus proteus X 19. No essential difference between the reaction of trachomatous and of nontrachomatous patients could be detected. Therapeutically, repeated injections of the vaccine had a beneficial effect in trachomatous patients, which was interpreted as being nonspecific, due to the foreign protein contained in the vaccine.

P. C. KRONFELD.

Tumors

ADRENAL NEUROBLASTOMA AND ITS OCULAR SYMPTOMS. H. S. KUHN, Am. J. Ophth. **22:** 642 (June) 1939.

Kuhn reviews the literature of neuroblastoma and reports a case in a 2 year old boy. He makes the following conclusions:

"As seen in the literature, reports of cases of adrenoblastoma with autopsies are very rare. In our case the ocular symptoms clinically resembled those that Hutchinson described as a significant group. The remarkable thing in this case is the tumor, which could not be located clinically but was first found at the autopsy located in the left adrenal. The tumor of the orbit, as is usual, was on the same side. In the x-ray examination, it appeared as a tumor of the base of the cranium with destruction of the bony orbit and its adnexa, especially the mandibular joint, forcing forward the eyeball.

"After removal of the orbital tumor the child was for a time in better condition, but he soon developed cachexia and died. The literature also indicates that removal of the tumor or treatment with radium or x-ray has a good influence on the patient's general health, but that a permanent result has never been obtained. Until now only radium or x-ray treatment of the primary tumor has been attempted. It has never before been removed surgically.

"It was very difficult to arrive either clinically or histologically at the correct diagnosis. Differential diagnoses to be mentioned are sarcoma and retinoblastoma. In their arrangement, the round cells resembled a round-cell sarcoma, and this diagnosis was made first, but soon corrected, and the tumor was identified as belonging to the group of tumors of the nervous system. The cells contained relatively much protoplasm, and there was hardly any intercellular substance. Larger cells were present, especially the ganglion type of cells and some rosettes. These findings led to the diagnosis of a neuroblastoma. As the eyeball and the optic nerve were not primarily affected by the tumor, but only secondarily, only a neuroblastic tumor could have been present, the origin of which is nearly always the sympathetic nervous system.

"The clinical events and the autopsy finally confirmed these conclusions."

W. S. REESE.

PRIMARY ANGIOMA OF THE SEMILUNAR FOLD. G. COLOMBO, Ann. di ottal. e clin. ocul. **67:** 550 (July) 1939.

Of 6 cases of angioma of the semilunar fold cited in the literature, the lesion in 2 was really telangiectasis; in 2 an angiofibroma and in 1, a transition-stage between angioma and angiofibroma. Only 1 case of true angioma of the semilunar fold, that of Bock, was found. The author's patient was a woman of 35 who had noted the growth for only three weeks. It was the size of a small pea and pedunculated and had bled spontaneously five days before. After excision and cauterization of the base, no recurrence was seen after one and a half years. Sections showed a pure angioma, probably of the arterial type. A photograph, three photomicrographs and a bibliography are included.

S. R. GIFFORD.

KERATOKERAS (HORN OF THE CORNEA). K. ORLOFF, Vestnik oftal. **15:** 6, 1939.

A horny tumor of the skin of the lid is rare, and such a tumor of the cornea is still rarer. A case of the latter condition is reported. A man aged 71 presented an ectatic, firm, brownish, horny tumor of the right cornea. Evisceration was done; during the operation the anterior segment of the tumor fell off and broke up into small pieces of layer-like tissue. A detailed histologic description is given. There was a gradual transition of the epithelial cells of the cornea into a homogeneous corneal tissue, with the layers increasing in numbers. Accumulated dust (the eye could not be closed) gave the brown color of the tumor.

O. SITCHEVSKA.

Uvea

EPIDEMIC PAROTIDITIS AND CHOROIDITIS. R. LAJE WESKAMP and CARLOS NOCCALANDRO, Arch. de oftal. de Buenos Aires **14:** 193 (Feb.) 1939.

A case is reported in which choroiditis made its appearance just prior to the outbreak of parotiditis. The case is fully studied, with the exclusion of other possible etiologic factors, including Heerfordt's parotiditis, and was complicated with mild meningitis.

C. E. FINLAY.

Vision

THE DOUBLE EYE. F. WECKERT, Arch. f. Ophth. **140:** 372, 1939.

The term "double eye" is used by the author to stress the intimate cooperation for which the two eyes with their nervous pathways and visual centers are intended. The cooperation consists of the complete fusion of corresponding retinal images. Normally this fusion is "rendered frictionless" by the approximately equal sharpness of the two retinal images, by the approximately normal refraction of the two eyes and by a perfect muscle balance. Abnormalities with regard to any of these three factors or insufficient "vital energy" of the fusion mechanism may lead to strabismus. The author accepts Grimm's definition of fusion (*Klin. Monatsbl. f. Augenh.* **101:** 758, 1939) as being the psychic process of coalescence of retinal impressions in which are entailed psychooptical reflex movements of the eyes. The development of torticollis in congenital palsy of the superior oblique muscle is a good illustration of the efficacy and strength of a normal fusion apparatus.

There are hereditary and acquired forms of fusion weakness. The latter may be caused by any systemic disease. The result of acquired failure of fusion is always the alternating form of strabismus with good vision in each eye.

Early occlusion of the squinting eye not only improves the visual function but reduces the angle of squint.

It is misleading to stress the presence of a central scotoma in a squinting eye. Actually, the function of the entire retina of the squinting eye is depressed. Harms's work on the pupillomotor sensitivity of central and paracentral retinal areas in squint (German Ophthalmological Society, 1938) is criticized. According to Weckert, amblyopic eyes have normal macular pupillomotor sensitivity.

P. C. KRONFELD.

THE DOUBLE EYE: COMMENT ON WECKERT'S ARTICLE. S. HARMS, Arch. f. Ophth. **140:** 589, 1939.

"The fundamental fact which Weckert does not consider in his discussion of binocular vision in squint is that the patient with strabismus almost always makes use of impressions received with both eyes." Instead of the normal binocular cooperation whereby the impressions received by corresponding or horizontally disparate retinal areas are combined into a single impression with depth value, acquired abnormal correspondence of the two retinas and inhibitory processes in the visual pathway prevail in strabismus. "Weckert apparently does not know the phenomenon of anomalous retinal correspondence." Harms cites from his own work and from that of Lo Cascio and Ziering the results of monocular and binocular perimetry in cases of strabismus, viz., the various forms of suppression scotomas. Amblyopia is the result of lasting suppression. Weckert's criticism of Harms's work on macular and paramacular pupillomotor sensitivity in squint amblyopia would be just only if Weckert had used Harms's method of determining pupillomotor sensitivity.

P. C. KRONFELD.

THE DOUBLE EYE: REPLY TO HARMS'S COMMENT ON WECKERT'S ARTICLE. F. WECKERT, Arch. f. Ophth. **140:** 595, 1939.

Weakness of fusion is the "key to the problem of strabismus." The mode of binocular cooperation in strabismus is not that of regional inhibition but the "fading away and annulment" of the entire "weaker" retinal image. In squint amblyopia no element of the optic nerve conducts properly. The behavior during reading of an eye with true central scotoma is fundamentally different from that of an eye with squint amblyopia.

P. C. KRONFELD.

Sympathetic Ophthalmia

SYMPATHETIC OPHTHALMIA. J. P. JENSEN, Acta ophth. **17:** 388, 1939.

Three hundred and seven perforating lesions of the eye were treated at the Kommune Hospital, Copenhagen, Denmark, during the ten years from 1927 to 1936. Five cases are reported in which the lesion clinically resembled sympathetic ophthalmia but in which no histologic examinations were made. A curious feature of 4 of these cases was that the condition occurred anywhere from three months to four years after the enucleation of the injured eye.

O. P. PERKINS.

Therapeutics

ETHYLMORPHINE HYDROCHLORIDE FOR TREATMENT OF DISEASES OF THE EYE. S. SUKHOV, Vestnik oftal. **15:** 18, 1939.

Suchov employed subconjunctival injections of a 3 to 6 per cent solution of ethylmorphine hydrochloride; 20 injections of 0.2 to 0.6 cc. were given every other day. Thirty patients were treated, chiefly those suffering from opacities in the vitreous, central chorioretinitis, hemorrhages in the retina associated with sclerosis of the retinal vessels and detachment of the retina (3 cases). Negative results were obtained in the last group, while in all the others the therapy gave good results, as the opacities in the vitreous cleared and the retinal hemorrhages absorbed after several injections.

The action of the ethylmorphine hydrochloride is due to dilatation of the blood vessels with the accompanying lymphogenic action which aids the nutrition of the tissues and the absorption of the inflammatory products.

The intraocular tension was not influenced by the injections.

O. SITCHEVSKA.

Society Transactions

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SECTION ON OPHTHALMOLOGY

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April 18, 1940

Hand-Schüller-Christian Syndrome: Report of a Case. DR. EUNICE STOCKWELL.

The patient was a 3½ year old white boy who had been well for the first year and a half of his life except that he had presented a feeding problem in his early weeks. At the age of 18 months the child had had whooping cough, and since then he had remained emaciated, sickly and irritable. During the same period (winter) yellow crusty lesions developed on his scalp, which improved only after roentgen therapy. His gums became swollen, spongy and tender. The teeth were loosened in their sockets, many being lifted out. During this same period a yellow viscid discharge developed in his left ear, and it is believed that he has been deaf since that time. Somewhat later diabetes insipidus developed and has continued up to the present time. He has had continuous enlargement of the skull with rarefaction. Because of progressive exophthalmos the child is now unable to close his eyes and so has keratitis due to exposure.

The condition has progressed, with little improvement from roentgen therapy. Otherwise the treatment has consisted of general supportive measures. The prognosis is poor.

DISCUSSION

DR. JOSEPH STOKES: Dr. Fewell and Dr. Stockwell know a great deal more about this condition than I do. It is of interest that Dr. Stockwell mentioned Dr. Alfred Hand, of Philadelphia, who first described this syndrome. It was in 1891, before the Pathological Society, that he presented his first observations of such a case at the Children's Hospital. The pathologist had said that it was a case of tuberculosis, but Dr. Hand stated that he felt that it was not tuberculosis but a disease not as yet described. The roentgen picture characteristic of the disease was described by Schüller in 1916, and Christian collected a large group of cases in 1919, describing particularly the signs and symptoms referable to the pituitary.

Rowland, perhaps more than any one else, beginning in 1928, has published studies which have shown the disease to be one probably of disturbance of lipid metabolism. No great contributions have been made, to my knowledge, since his earlier work, nor has the true cause been

determined. The condition has, as one can readily see, prominent manifestations, including chiefly changes in the bones of the skull and the pelvis. In many of the cases, too, there is marked dwarfism; it is fortunate that in many the condition is self limited. Although the patients remain dwarfed, they have no serious mental defect, and physically, except for their dwarfism, they are in good condition. I had hoped that by means of roentgen treatment of this child a regression in the symptoms could be brought about, but, as Dr. Stockwell has said, even with doses of 200 r. there has been no great change. Pituitary preparations have been tried for the dwarfism, without a great deal of success.

DR. MARY BUCHANAN: I should like to know whether those patients live long.

DR. WARREN REESE: Is there any explanation for the exophthalmos?

DR. FRANCIS HEED ADLER: I should like to ask whether Dr. Stokes means by regression that the exophthalmos recedes? Do children ever recover from this disease? In this instance the exophthalmos seems to be of the malignant type, and if the child is going to live something may have to be done to preserve the eyes. Would it be advisable to consider decompressing one of the orbits?

DR. EUNICE STOCKWELL: In answer to Dr. Buchanan, these conditions usually terminate in starvation and anemia. The exophthalmos is caused by the decomposition of the fatty substances in the orbit. I think that one could remove the eye, but in that event one would have all the other substances to account for.

DR. FRANCIS HEED ADLER: I surmised from what Dr. Stokes said that in some of these children the disease stops and recovery occurs.

DR. JOSEPH STOKES: I have seen a number of cases in which this occurred, but none in which this degree of exophthalmos was present. The danger of decompression lies in the danger of secondary infection. I have seen an instance in which there was a draining sinus from the pelvis for months. There is great danger in any operative procedure, though something may have to be done in this case. I should like to know whether any one has seen exophthalmos of this degree, because I think that it is comparatively rare. I have observed cases in which this condition was mild and not progressive and which have not been reported.

DR. LAWRENCE M. WEINBERGER: It is, of course, possible to take off the roof of the orbit for any form of exophthalmos. However, in the presence of xanthomatosis the orbits are filled with granulomatous lipoid masses that continue to expand and infiltrate the surrounding bone, so that even though one did remove it it would only be a question of time till the further accumulation of these masses had made the situation much as it was before.

Primary Pituitary Adenoma: Report of a Case. DR. LAURENCE M. WEINBERGER.

DISCUSSION

DR. FRANCES HEED ADLER: It seems a long way from the days when the diagnosis of tumor of the brain was made on the basis of headaches, vomiting without nausea and choked disk. The more one learns about tumors of the brain the more obvious it becomes that they may give rise

to any symptoms whatsoever relating to intracranial pathologic change. I think that if any physician were faced with the histories of some of these cases, especially those in which there is sudden pain in an eye with proptosis and ptosis, the last thing he would think of would be pituitary adenoma. I am sure that aneurysm would come to his mind first. It is obvious that this paper is very instructive, even though it does not deal with the usual run of pituitary tumors. Although one still can adhere to the old textbook pictures, one must keep in mind the fact that pituitary lesions can cause symptoms which are somewhat far afield from the site from which the tumor grows.

Dr. Leo F. McAndrews: What is the explanation of the sudden onset of pain? Is it due to the thrombosis of the cavernous sinus? I have a patient (whom Dr. Grant has seen) who has a pituitary lesion. She has no complaints—no headaches, though a gradual loss in the visual fields has been found. Her case confirms what has been said, that the patient may not have any of the typical symptoms of tumor of the brain.

Dr. James S. Shipman: How can one account for a sudden onset of pain if the tumor has been pressing on the trigeminal nerve for so long? In how many of these 169 cases was papilledema found?

Dr. Laurence M. Weinberger: The reason for the sudden onset of pain, I must confess, is just as much unknown as the reason for sudden onset of ptosis or ophthalmoplegia. The suddenness of it makes one conjure up some vision of the tumor rupturing into the cavernous sinus, but this seems rather unlikely.

Dr. Francis Heed Adler: Can you give any explanation of the papilledema mentioned in these cases?

Dr. Laurence M. Weinberger: I am sorry that I cannot account for the papilledema. Papilledema in our series of cases was not particularly rare. I suppose that in the cases observed from 1910 to 1920 it was more frequent than has been noted in later years, because the patients were then allowed to wait longer before operation. I think I have seen 15 or 16 cases of papilledema varying from slight to 6 or 8 D. It is interesting to note that Cushing and Walker, a number of years ago, pointed out that 20 per cent of their patients with pituitary adenomas did not have visual symptoms of any kind. I think that ophthalmologists should keep this point in mind, for one does not necessarily need evidence of injury of the chiasm to make the diagnosis, and if one waits for such evidence one may wait too long.

Congenital Colobomas of the Lower Lid. Edmund B. Spaeth.

Three children of one family all had similar defects of the lower lids, the only differences being in the degree of involvement and in the amount of pathologic changes about the puncta, canaliculi, lacrimal sacs and nasal ducts.

The cases were presented from the standpoint of etiology and to demonstrate the surgical technic required, outlined and utilized for maximum correction.

DISCUSSION

Dr. James S. Shipman: I feel that Dr. Spaeth deserves a great deal of credit for his optimism and his perseverance, and I think that he should be congratulated on his results in these 3 cases.

DETROIT OPHTHALMOLOGICAL SOCIETY

PARKER HEATH, M.D., *President*

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April 18, 1940

Virus Disease of the Eye. DR. PHILLIPS THYGESON, New York.

Viruses have been defined as infectious agents of disease which cannot be classified as bacteria, fungi, protozoa, spirochetes or rickettsias and which in size lie near or below the limits of resolution of the compound microscope. They have three main characteristics which distinguish them from other microbic forms: 1. They pass filters which retain ordinary bacteria. 2. They are unable to develop apart from living cells. 3. Most of them produce inclusion bodies in the nuclei or cytoplasm of affected cells. Since the initial discovery by Iwanowsky in 1892 of the virus of tobacco mosaic, a large number of viruses have been isolated; many of them have great hygienic and economic significance.

Only a few viruses, for example, trachoma virus, attack the eye only; the majority which attack the eye affect other structures of the body as well. Among these are the viruses of herpes simplex, herpes zoster, molluscum contagiosum, the common wart, vaccinia, variola and lymphogranuloma venereum. Other viruses, such as those of influenza, varicella and foot and mouth disease, produce ocular lesions only rarely.

In addition to the known virus diseases, there are a number of ocular diseases in which a virus is suspected of being the causative agent but proof has not been obtained. These include ocular pemphigus, chronic follicular conjunctivitis, acute follicular conjunctivitis (Beal), superficial punctate keratitis, pseudotumor, some types of uveitis and periodic ophthalmia of horses.

Virus diseases in general are resistant to therapy, but three ocular virus diseases, namely, trachoma, inclusion blennorrhea and lymphogranuloma venereum, respond favorably to treatment with sulfanilamide or its derivatives.

Ocular Complications in Myasthenia Gravis. DR. LELAND CARTER.

Three women with myasthenia gravis were also found to have complete bilateral external ophthalmoplegia. They presented similar characteristics. The onset of the disease was in youth, at the age of 15, 16 and 20 years, respectively. The duration of the disease was four, eighteen and twenty-six years, respectively. Graefe's prism test showed only a few degrees of movement in any field of action. Examination showed bilateral ptosis, paralysis of convergence, myopic astigmatism, normal visual fields and normal eyegrounds.

Book Reviews

Die bösartigen Geschwülste des Auges und seiner Umgebung. A Series of Addresses by R. Grashey, W. Rohrschneider, R. Thiel and J. Zange, presented at the ninety-fifth meeting of the Society of German Scientists and Physicians, Stuttgart, 1938. Edited by R. Thiel. No. 6 in Bucherei des Augenarztes, supplement to Klinischen Monatsblätter für Augenheilkunde, 1939. Price, 7 marks. Pp. 106, with 122 illustrations. Stuttgart: Ferdinand Enke, 1939.

This monograph contains a series of articles on malignant tumors of the eye and of its surroundings. The first article by W. Rohrschneider, an authority on this subject, considers the lesions of the eye caused by roentgen rays and radioactive substances, and their prevention. Although the problems of dosage, including the damaging dose, cannot be considered as settled, it is evident that progress has been made along this line, a subject to which the author has made valuable contributions.

An important part of the monograph is by R. Thiel on diagnosis and treatment. It is divided from an anatomic standpoint into chapters on tumors of the lids, conjunctiva and cornea, on intraocular growths and on tumors in the retrobulbar and retro-orbital regions. The more common facts are stated with brief accuracy and are illustrated by schematic drawings and by a selection of excellent reproductions in black and white and in color. A number of pertinent case reports are added. On the question of surgical or roentgen treatment, the majority of oculists will agree with Thiel's standpoint, that as long as abundant experience with radiotherapy is not available, surgical treatment of the lids, conjunctiva and cornea seems to be the method of choice. In the chapter on tumors in the retrobulbar and retro-orbital areas, orbitography, a diagnostic method employing colloidal thorium dioxide, suggested by Thiel, is mentioned. Arteriography is shown as a valuable aid in the diagnosis of retro-orbital tumors and for the differential diagnosis between these growths and inflammatory changes and vascular lesions in the middle cranial fossa.

R. Grashey gives a short and instructive survey of the indications for radioactive therapy in diseases of the eye and its neighborhood from the point of view of the radiologist. As a specialist equipped with large experience and thorough technical knowledge of the subject, he may accomplish exceptionally good results. Another point well worth mentioning is the correction of the faulty conception held by many people of the stimulating action of roentgen rays on tumor cells.

The last article, on diagnosis and treatment of malignant growths of the nose and the eye, is by J. Zange. The limits of some of the principal procedures are explained. The description of the diagnostic value of the cloudiness of sinuses and of orbit and the arguments in favor of superiority of electrosurgery in special cases are useful. Case records and good illustrations complete the text.

This last number of the "Bücherei des Augenarztes" has greater practical value than any of the former publications in this collection.

L. SALLMANN.

Die pathologische Histologie der Tränendrüse. By Dr. Magda Radnot. Price, 7.80 Swiss francs. Pp. 64, with 14 illustrations. No. 28 of Bibliotheca Ophthalmologica, Supplement to the Ophthalmologica. Basel: S. Karger, 1939.

This short monograph on the histopathology of the tear gland is based on the author's extensive investigations. The upper tear glands obtained at 500 autopsies in addition to biopsy specimens were studied. These findings are compared with those reported in the literature and give a full description of the different phases of the histologic changes in normal and diseased glands.

The division into twenty chapters with some subdivisions does not make for organic coherence but facilitates consultation by the reader. With reference to the histologic changes, the chapter on onkocytes is of interest, although the pathologic significance of these cells is not clear. The description of the development of clusters of lymphocytes in the normal gland, the death of epithelial cells and the process of atrophy will be appreciated by the pathologist who deals principally with biopsy specimens. Emphasis must be placed on the author's opinion that the histologic changes which Sjögren believes to be characteristic of keratoconjunctivitis sicca are not of inflammatory or specific nature. Several good photomicrographs conclude this valuable study.

L. VON SALLMANN.

Das Schielen und seine Behandlung. Paul A. Jaensch. Bücherei des Augenarztes. Beihefte der Klinischen Monatsblätter für Augenheilkunde, no. 4. Price, 4.60 marks. Pp. 44, with 27 figures and 2 tables. Stuttgart: Ferdinand Enke, 1938.

The author attempts to give within a limited space a survey, intended for the ophthalmologic practitioner, of the knowledge pertaining to concomitant strabismus. The fundamental physiologic concepts which, since set forth by Hering and Bielschowsky, have formed the basis for the understanding of the pathologic phenomena of squint, are touched on in a few sentences. The procedures to be followed in the examination of patients are then discussed, and the forms and causes of latent and manifest convergent, divergent and vertical strabismus are described. The author next lays down the principles of conservative and orthoptic treatment of these various forms and devotes the last chapter to the operative treatment of squint. Jameson's recession and Verhoeff's suture for advancement are mentioned.

The value of this brief exposé is, necessarily, restricted. The presentation is too concise to be sufficiently detailed for any one not thoroughly familiar with this difficult subject; the beginner who desires to understand, diagnose and treat strabismus will have to refer to more elaborate treatises, while for the one well versed in the subject the booklet does not bring anything new.

HERMANN M. BURIAN.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

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President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

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Secretary: Dr. K. O. Granström, Södermalmstorg 4 IIII tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Albert C. Snell, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

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Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.

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Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

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Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

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Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.
Executive Director: Mrs. Eleanor Brown Merrill, 50 W. 50th St., New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. V. May, 1703 Main St., Marinette.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Wisconsin Rapids. Time: June 1941.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles, Calif.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clarence W. Shannon, 4th and Pike Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1215–4th Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. E. Rideout, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

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Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

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Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

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President: Dr. J. K. Heckert, 103 N. Washington St., Lansing.
Secretary-Treasurer: Dr. W. D. Irwin, 710 Hanselman Bldg., Kalamazoo.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

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President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. W. E. McClellan, 750 Main St., Hartford.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.
Place: Macon. Time: May 13-17, 1941.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
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Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
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Minnesota Academy of Ophthalmology and Otolaryngology

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Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

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Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.
Place: Atlantic City. Time: June 3-5, 1941.

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Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

North Carolina Eye, Ear, Nose and Throat Society

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Secretary-Treasurer: Dr. M. R. Gibson, Professional Bldg., Raleigh.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. W. Carpenter, 200 E. North St., Greenville.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. J. W. Ward, 2607½ Lee St., Greenville.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
Place: Fort Worth. Time: Dec. 13-14, 1940.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 628 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Pliace: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Richard Gamble, 30 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert D. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. J. Charles Dickson, 1617 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. J. M. Masters, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Leonard C. Whiting, 121 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.
Secretary: Dr. Brittain Payne, 35 E. 70th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr. Morris Davidson, 80 Centre St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. Howard Heine, 635 N. Main St., Fremont, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward A. Weisser, 119–5th Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Edwin S. Ingersoll, 26 S. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 8 p. m., second Wednesday of each month from September to May.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Matthew Hosmer, 384 Post St., San Francisco.
Secretary: Dr. Fred Boyle, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Conner Moss, 1710 Rhode Island Ave. N.W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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